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

Summary Report

November 6-7, 2024

Atlanta, Georgia

Contents

RECORD OF ATTENDANCE

The Committee shall consist of up to 20 members, including the Chair, and includes a non-voting liaison representative who is a member of the Advanced Medical Technology Association (AdvaMed). CLIAC also consists of three non-voting ex officio members or designees from CDC, CMS, and FDA. The Designated Federal Officer (DFO) ensures procedures comply with applicable statutory, regulatory, and HHS General Administration Manual directives. Visit https://www.cdc.gov/cliac/php/members/index.html to find a list of the current CLIAC members, including a brief overview of their applicable expertise.

Committee Members Present

Dr. Jordan Laser (Chair)
Dr. Esther Babady
Mr. Michael Black
Dr. Olga M. Cerón
Dr. Kimberle Chapin
Dr. James Crawford
Ms. Heather Duncan
Dr. Mary Edgerton
Dr. Tanner Hagelstrom
Dr. Yael Heher
Dr. Soojin Jun
Dr. David Koch
Dr. Hung Luu
Dr. Nirali Patel
Dr. Michael Pentella
Dr. Anthony Tran
Dr. Mark Tuthill
Dr. R.W. (Chip) Watkins
Ms. April Veoukas, AdvaMed (Liaison Representative)

Committee Member Absent

Dr. Chester Brown

Ex Officio Members

Dr. Víctor R. De Jesús, CDC
Mr. Gregg Brandush, CMS
Dr. Courtney Lias, FDA

Designated Federal Officer and 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 attended via virtual Zoom webcast, and approximately 160 public citizens attended 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 and to establish advisory committees under Section 222.

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 about 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 microbiology, immunology, chemistry, hematology, and pathology and representatives of medical technology, public health, clinical practice, and consumers. In addition, CLIAC includes three ex officio members, or designees: the Director of the Centers for Disease Control and Prevention (CDC); the Commissioner of the Food and Drug Administration (FDA); the Administrator of the 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.

Because 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. Jordan Laser, CLIAC Chairperson, welcomed the Committee and recognized Dr. Collette Fitzgerald's accomplishments during her term as the CDC Ex Officio. After thanking Dr. Fitzgerald, he provided an overview of Dr. Reynolds Salerno's term and thanked him for his tenure as the CLIAC Designated Federal Officer (DFO). Dr. Reynolds Salerno, the Director of the Office of Laboratory Systems and Response (OLSR), acknowledged the importance of CLIAC and thanked past and current members of the Committee. He introduced Ms. Heather Stang, Senior Advisor for Clinical Laboratories in CDC's Division of Laboratory Systems (DLS) in OLSR, as the new CLIAC DFO, and Dr. Víctor R. De Jesús, Acting Director of DLS, as the new CDC EX Officio. Ms. Stang welcomed the Committee and the members of the public. Dr. Jordan Laser, CLIAC Chairperson, welcomed the Committee and reviewed the process for public comments, quorum requirements, and official CLIAC recommendations. Ms. Stang introduced the new CLIAC members, and all members made self-introductions and financial disclosure statements relevant to the meeting topics. Dr. Laser stated that the agenda topics would include CDC, CMS, and FDA agency updates. In addition, the meeting would consist of presentations and discussions on two workgroup reports, cybersecurity requirements in the clinical laboratory, the determination of clinically relevant range of values for proficiency testing, and the utilization of remote technology for competency assessments.

Recognition of Outgoing CLIAC Members

Heather L. Stang, MS, MLS
Senior Advisor for Clinical Laboratories
Division of Laboratory Systems
Office of Laboratory Systems and Response
Centers for Disease Control and Prevention
Presentation 1

Ms. Stang recognized Ms. Heather Duncan for her contributions to the Committee.

AGENCY UPDATES AND COMMITTEE DISCUSSION

Centers for Disease Control and Prevention (CDC) Update

Víctor R. De Jesús, PhD
Acting Director, Division of Laboratory Systems
Director, Quality and Safety Systems Branch
Office of Laboratory Systems and Response
Centers for Disease Control and Prevention
Presentation 2

Dr. De Jesús provided a comprehensive update on the CDC's Division of Laboratory Systems (DLS), highlighting organizational changes and ongoing projects. He discussed the realignment of several CDC divisions into the new Office of Laboratory Systems and Response (OLSR) to improve coordination and efficiency, focusing on establishing a robust laboratory infrastructure for public health. Dr. De Jesús outlined key DLS activities, including laboratory quality and safety efforts, diagnostic excellence, workforce development, data science, and health equity. Notable projects included revising educational materials for the waived testing community, the Next Generation Sequencing (NGS) Quality Initiative, and the ECHO Biosafety Program. He also provided updates on the CDC's laboratory readiness and response efforts, including the Laboratory Response Network for Biological Threats (LRN-B), which ensures laboratories are prepared for biological threats. Dr. De Jesús emphasized the importance of the Laboratory Outreach Communication System (LOCS), which provides up-to-date testing and emergency response information to approximately 90,000 subscribers. He also highlighted a significant achievement: awarding an Indefinite Delivery Indefinite Quantity (IDIQ) contract to support surge testing and data sharing, which several CDC centers have already utilized. He discussed the OneLab™ initiative, which has grown significantly, reaching over 41,000 members and offering training and resources to laboratory professionals. He also mentioned the development of the CLIA Laboratory Director University (LDU) program in collaboration with CMS, which aims to address training requirements for laboratory directors. Additionally, Dr. De Jesús updated CLIAC on the SHIELD initiative, which focuses on improving interoperability of laboratory data and ongoing collaborations with CMS to automate the transfer of laboratory-related data into the CDC's data lake. Lastly, Dr. De Jesús shared updates on initiatives promoting health equity in laboratory systems, including the Electronic Test Orders and Results (ETOR) project, which aims to improve

data exchange in underserved areas, and the LDL laboratory messaging project in collaboration with the Million Hearts® Initiative. He concluded by providing an update on the Career Pathways in Public Health Laboratory Science program, which seeks to increase diversity and inclusion in laboratory fields to place more fellows and interns from underrepresented groups.

Centers for Medicare & Medicaid Services (CMS) Update

Gregg S. Brandush, RN, JD
Director
Division of Clinical Laboratory Improvement and Quality
Quality, Safety, and Oversight Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
Presentation 3

Mr. Brandush began by highlighting the leadership team of the CMS Division of Clinical Laboratory Improvement and Quality (DCLIQ), which includes two policy branches and three operations branches, all restructured to align with DCLIQ's primary activities. He reported that while the organization has made progress, efforts to address communication issues remain ongoing as the structure settles. He then reviewed the current laboratory enrollment in the CLIA program based on certificate type, noting that Certificate of Waiver (CoW) sites continue to account for 81% of all CLIA-certified laboratories. Mr. Brandush also highlighted progress in enforcement actions, noting significant improvements in reducing the time it takes to address non-compliance. The time to initiate and impose sanctions has been reduced by more than 50%, a substantial improvement from previous years. He noted that this has helped ensure quicker action against laboratories with serious non-compliance issues, enhancing the overall quality of testing. Mr. Brandush then provided updates on several goals for 2024, including making 50% of CLIA certificates available electronically, issuing new interpretive guidance, and addressing inconsistencies related to survey processes. He also emphasized ongoing efforts to ensure full electronic processing of certificates by 2026 and efforts to eliminate survey backlogs. Notably, the organization has reduced backlogs by 33% over six months, an accomplishment made possible through collaboration with state agencies and federal surveyors. Lastly, he mentioned several policy updates and administrative memos, including technical corrections to analyte categorization and new certifications for cytotechnologists.

Food and Drug Administration (FDA) Update

Courtney H. Lias, PhD
Director
Office of In Vitro Diagnostic Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health
U.S. Food and Drug Administration
Presentation 4

Dr. Lias opened her presentation by highlighting key developments in diagnostic testing. She emphasized the FDA's ongoing efforts to expand home-use testing, a priority amplified by the COVID-19 pandemic. Home tests, she explained, offer greater privacy and convenience and help reduce the spread of infectious diseases. Dr. Lias outlined the FDA's work to optimize regulatory pathways for certain diagnostic tests, including the recent down-classification of Hepatitis B and CMV assays, which now qualify for less stringent approval processes. She also addressed the FDA's response to avian influenza, noting collaborative efforts with the CDC, NIH, and other partners to evaluate the effectiveness of current influenza A tests in detecting avian strains. Regarding COVID-19 testing, Dr. Lias highlighted the FDA's push to transition emergency use authorized (EUA) tests to traditional marketing pathways to ensure long-term availability. She announced that the FDA revoked Cue Health's EUA for COVID-19 tests in October due to an increased risk of false results. Dr. Lias shared updates on advancements in hepatitis C diagnostics, including authorizing a point-of-care molecular test, which supports the "test-to-treat" initiative and improves treatment access for underserved populations. She also highlighted significant approvals in home-use testing since the last meeting. Regarding colorectal cancer screening, Dr. Lias noted the approval of three new tests in October, providing improved options for average-risk individuals and supporting efforts to increase screening rates. She affirmed the FDA's commitment to improving access to diagnostic tests and advancing public health initiatives.

PRESENTATIONS AND COMMITTEE DISCUSSION

CLIAC Workgroup Reports

The Biosafety Workgroup Report

Michael A. Pentella, PhD
Director, State Hygienic Laboratory
The University of Iowa
Presentation 5 and Workgroup Report 5a

Dr. Pentella, Chair of the CLIAC Biosafety Workgroup, reminded the members of the five CLIAC recommendations made between 2001 and 2019 that address laboratory safety. He provided the workgroup charge, membership, scope, and discussion topics. Dr. Pentella highlighted the workgroup's discussions on the questions and reviewed the workgroup agreements related to biosafety and the need to update the CLIA requirements to include additional safety standards to ensure laboratories have policies and procedures addressing laboratory biosafety.

Public Comments

No public comments were received on this topic.

Committee Discussion

The Committee discussed the workgroup agreements summarized in the CLIAC Biosafety Workgroup presentation and report. Relevant CLIAC member comments follow.

- A member asked how a risk assessment can be performed before purchasing a new piece of equipment when the equipment is not on site. The workgroup chair clarified that conducting a risk assessment before purchasing equipment would be a theoretical process involving a review of the test procedures for the instrument and thinking through the steps to identify potential risks and hazards.
- Another member asked whether the workgroup's focus is on biosafety risk assessments for instrumentation specifically or if it applies to general laboratory biosafety and expressed concerns about potential conflicts between instrument handling and decontamination procedures and existing safety. The workgroup chair confirmed that the workgroup was focused on instrumentation and its associated risks. He emphasized that general information on what a risk assessment entails would benefit the entire biosafety plan.
- Another member asked whether the risk assessment for equipment and instrumentation would be similar to the pathogen-specific or methodology-specific risk assessments currently conducted. The workgroup chair clarified that the workgroup is focused on instrumentation risk assessments for the entire laboratory.
- Several members discussed the intention to incorporate risk assessments into the CLIA regulations, ensuring that audits will include evaluations of risk assessments, individual competencies, and biosafety practices, thereby making the audits more comprehensive than they are currently. Members commented that any regulation changes should not result in an excessive burden on laboratories.
- The FDA Ex Officio informed the Committee that they are exploring opportunities to work with partners to address requirements for manufacturers to add information on the disinfection of instruments to their labeling or as part of their instrument instructions and noted that the FDA’s requirements for manufacturers are under the Federal Food, Drug, and Cosmetic Act and are not subject to CLIA and therefore are out of scope for CLIAC discussions.
- Several members discussed that laboratories should conduct their own risk assessments. However, risks related to aerosolization inside instruments, for example, are not something end users would typically be aware of, and this information must come from the manufacturers.
- Several Committee members discussed the potential burden of requiring laboratory biosafety risk assessments. There was broad consensus that by clearly defining the components of the risk assessment, it would be possible to standardize laboratory practices and streamline the process, making it more manageable for laboratories to implement. The goal is to educate and train laboratory personnel while simplifying the process of conducting biosafety risk assessments to facilitate compliance.
- Members agreed on the need for a form, training document, or webinar to provide laboratories with clear guidance on conducting biosafety risk assessments.

- Several CLIAC members expressed concerns regarding competency assessments for conducting risk assessments. It was agreed that the intention is to establish a general biosafety competency that would apply to all instrumentation used within the laboratory instead of each instrument.

Committee Recommendations

The Committee deliberated, voted, and approved the following recommendations based on the topic of *The CLIAC Biosafety Workgroup Report*.

Recommendation 1: CLIAC recommends revising the CLIA requirements to include general biosafety training as part of the competency requirements for testing personnel.

Recommendation 2: CLIAC recommends that a standardized definition of a biosafety risk assessment should be developed and added to 42 CFR 493.2.

a. The language used to define a biosafety risk assessment should cover general biosafety risk assessment processes, including hazard assessment, mitigation, management, and performance monitoring.
    i. Part of the general biosafety risk assessment could include a request, if available and provided, and written equipment disinfection instructions and practices, preferably before purchase.
    ii. Laboratories should consider the provision of written disinfection instructions and practices before purchasing equipment.

Recommendation 3: CLIAC recommends that CDC provide educational tools and resources on how laboratories can develop and perform biosafety risk assessments.

Recommendation 4: CLIAC recommends that it is best practice that laboratories should be required to perform a biosafety risk assessment on all instrumentation currently in use. Before implementation, laboratories should consider biosafety risks when purchasing new equipment and must complete a risk assessment (analogous to analytic verification).

Recommendation 5: CLIAC recommends that 42 CFR 493.1804(a)(2) should be expanded to clarify that laboratory workers and, in turn, the general population should be safeguarded.

The Next Generation Sequencing Workgroup Report

Nirali M. Patel, MD
Senior Pathologist
Tempus Labs
Presentation 6 and Workgroup Report 6a

Dr. Nirali Patel began with a brief history that led to the workgroup formation and explained that the charge was to make suggestions to qualify bioinformatics personnel as CLIA testing personnel in laboratories performing high complexity testing. She stated that the discussions were meant to focus on the minimum requirements for bioinformatics to be integrated into the clinical laboratory. She described the questions the workgroup was tasked to answer, the discussions the workgroup had, and the final workgroup agreements. She reiterated that the discussions were kept general to include future tests and technologies while keeping the focus on bioinformatics in the clinical laboratory. Dr. Patel described the suggested routes for bioinformaticians to qualify under CLIA based on the current CLIA requirements. These routes included education, educational requirements, experience, or a combination.

Public Comments

No public comments were received on this topic.

Committee Discussion

The Committee discussed the workgroup agreements summarized in the CLIAC Next Generation Sequencing Workgroup presentation and report. Relevant CLIAC member comments follow.

- Several committee members expressed concerns regarding the workgroup's proposal for educational requirements for bioinformaticians, specifically the agreement that candidates possess one to two years of experience in a clinical laboratory. They noted the already limited pool of qualified bioinformaticians and emphasized that such a requirement could further hinder recruitment efforts.

- Another concern raised by several Committee members was the impact of the proposed educational requirements on individuals with degrees in fields such as epidemiology and whether laboratories utilizing third-party vendors for bioinformatics analysis would be affected. Dr. Patel clarified that the laboratory experience requirement pertained to general laboratory work rather than bioinformatics-specific tasks and emphasized that the workgroup proposal for requirements was intended for personnel directly involved in CLIA-regulated patient testing and treatment rather than those engaged in surveillance activities. Additionally, it was noted that the forthcoming CLIA personnel rules, set to take effect at the end of 2024, employ a variety of qualification standards similar to those outlined by the workgroup. Dr. Patel further explained that third-party vendors currently operate outside the typical regulatory framework, with responsibility for vendor quality falling under the purview of the CLIA laboratory director.
- A Committee member suggested using the term “informaticist” instead of “informatician,” noting that the former is recognized by organizations such as the American Medical Informatics Association and the Pathology Informatics Association. The member also recommended including internships as an option for gaining laboratory experience and proposed narrowing the definition of bioinformatics to focus specifically on molecular diagnostics and laboratories. In response, Dr. Patel clarified that the workgroup agreed to use the term “bioinformatician.” Additionally, the CLIAC DFO explained that many informatics procedures discussed by the workgroup were classified as part of the practice of medicine and, therefore, fell outside the scope of CLIA, making an alternate term of “bioinformatician” preferable. Dr. Patel noted that the workgroup opted for a broader focus to accommodate potential future testing developments that may be relevant.
- A Committee member noted that in New York State, the term "profession" is a statutory designation applied to occupations requiring licensure. The member suggested that the workgroup might inadvertently be defining bioinformatics as a new profession and recommended that the Committee clarify whether it is establishing educational requirements for a position or defining a new profession.
- The FDA Ex Officio member questioned the phrasing "develop and modify" as part of the workgroup’s proposed bioinformaticians' responsibilities, suggesting it might imply activities beyond CLIA's regulatory scope, such as software design and development. Dr. Nirali Patel clarified that "develop and modify" referred to adjusting bioinformatics pipelines to accommodate changes like new specimen types or updated human genome builds, ensuring accurate analysis. The FDA Ex Officio recommended clarifying the language to distinguish between software use, which falls under CLIA, and software development outside its purview. The CLIAC Chair acknowledged the concern, suggesting that "develop" and potentially "modify" be reconsidered to avoid implying software design activities. The Chair also indicated a need to refine the wording and transition toward finalizing recommendations.
- A CLIAC member expressed concern that the proposed requirements could disadvantage laboratories by limiting access to already scarce bioinformatics resources, potentially forcing reliance on unregulated third-party vendors. The member noted a potential disparity: third-party vendors, which only provide data analysis and fall outside CLIA's purview, would be unaffected by the requirements, while in-house hires would face significant qualification barriers, creating additional challenges for laboratories. The CLIAC Chair questioned whether the requirements should explicitly address third-party vendors or focus solely on in-house bioinformaticians. Dr. Nirali Patel reiterated that external vendors are currently outside CLIA's regulatory authority, with laboratory directors responsible for assessing vendor quality. She emphasized that bioinformatics, as a discipline, is not formally under CLIA oversight. Dr. Patel clarified that the workgroup focused on formally integrating bioinformaticians into laboratory testing personnel to address gaps in recognition and oversight of their roles.
- A Committee member highlighted the complexity of the bioinformatician qualification issue and suggested that a doctoral or master’s research project could potentially qualify as relevant experience and proposed a more general approach to educational requirements, allowing flexibility for fields like statistical genetics. The member emphasized creating a list of required competencies for bioinformaticians, such as coding, developing proficiency testing plans, and updating software or libraries. They flagged the risks of software modification, suggesting it requires thorough testing akin to a laboratory-developed test or in vitro diagnostics approach, and inquired about the role of the FDA and HHS in regulating testing involving artificial intelligence (AI) technologies. The CLIAC Chair and members agreed on the need for general language encompassing various relevant biological and data sciences disciplines, acknowledging the lack of standardized nomenclature for degree titles.

Committee Recommendations

The Committee deliberated, voted, and approved the following recommendations based on the topic of *The CLIAC Next Generation Sequencing Workgroup Report*.

Recommendation 6: CLIAC recommends that the CLIA testing personnel qualifications for laboratories performing high complexity testing should be modified to add a qualification route for the responsibilities of bioinformaticians, which are not burdensome for laboratories.

Recommendation 7: CLIAC recommends that a CLIA personnel carve-out be created to allow individuals who perform bioinformatics data analysis to qualify under CLIA, similar to how the current blood gas analysis carve-out is at § 493.1461 and § 493.1489. This carve-out should be developed for all CLIA-required personnel in the clinical laboratory who are involved in bioinformatics.

Recommendation 8: CLIAC recommends using the existing CLIA personnel roles (testing personnel, general supervisor, technical supervisor, and director), along with the experience and degree requirements, as a framework to build upon.

- The bioinformatician qualification paths may include requirements for bioinformatics beyond biological and data sciences that may consist of specialized areas such as bioinformatics, genetics, statistics, statistical genetics, computer science, software engineering, biochemistry, etc.
- A carve-out would also be needed for general supervisors, technical supervisors, and laboratory directors who oversee bioinformatics activities in laboratories performing high complexity testing using the workgroup's proposal for bioinformatics testing personnel as the baseline.

Cybersecurity Requirements in the Clinical Laboratory

Introduction to Topic

Gregg S. Brandush, RN, JD
Director
Division of Clinical Laboratory Improvement and Quality
Quality, Safety, and Oversight Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
Presentation 7

Mr. Gregg Brandush provided an overview of the cybersecurity challenges facing healthcare organizations, noting that ransomware attacks accounted for 70% of successful cyberattacks, with over 1,600 health organizations affected in 2023 alone, costing an average of $11 million per breach. He highlighted the two key issues: compromised patient care due to inaccessible or attacked electronic health records and legal liabilities arising from compromised patient data. Mr. Brandush noted that current cybersecurity regulations within CLIA are minimal, and general regulations exist for test procedure manuals, test report standards, and equipment maintenance. Still, these do not specifically address cybersecurity threats. He added that recommendations from the National Computing Centre (NCC) include basic cybersecurity measures such as multi-factor authentication, segregating legacy systems, regular staff training, and incident management plans. Mr. Brandush closed by providing several questions for CLIAC to consider, including whether stronger regulatory requirements for cybersecurity protocols in laboratories are necessary.

Cybersecurity Considerations for Clinical Laboratories

David McClintock, MD
Chair, Division of Computational Pathology & AI
Department of Laboratory Medicine and Pathology
Mayo Clinic
Presentation 8

Dr. McClintock discussed the critical cybersecurity considerations for clinical laboratories, emphasizing the increasing prevalence of cyberattacks, including those targeting hospitals and children's hospitals. He highlighted that no laboratory is immune to these threats and outlined various types of security risks, focusing on six key areas: (1) social engineering involves tactics like phishing and spear phishing, where attackers exploit human emotions to gain access to sensitive information; (2) third-party exposure is another concern, as many labs rely on external systems that may have vulnerabilities, making it essential to assess the security of third-

party applications and middleware; (3) cyber hygiene, which includes user education, strong password policies, regular risk assessments, and secure backups, is crucial for enhancing cybersecurity posture; (4) cybersecurity controls, laboratories should implement both proactive cybersecurity controls, such as ethical hacking, and reactive strategies like firewalls and antivirus software to defend against attacks; (5) effective data management practices are necessary as digital pathology increases the risk of unauthorized access due to easily distributable data; and (6) post-attack procedures must be in place, as labs need specific response plans to address network outages and prioritize restoring critical systems after an attack. Dr. McClintock concluded by stressing the reality of cyber threats in laboratory settings and encouraged laboratories to actively integrate cybersecurity principles into their operations, underscoring the importance of preparation to mitigate the impact of potential attacks.

Public Comments

PC1: The College of American Pathologists (CAP)

Committee Discussion

- One member expressed surprise at a comment from the CAP regarding cybersecurity in laboratory computing, emphasizing that many current practices are inadequate and pose risks. The member highlighted challenges posed by federal regulations, particularly concerning FDA-certified devices that cannot receive security patches without risking their validity. The member noted concerns about laboratories transmitting data in clear text over networks. The member advocated for best practices and the potential need for CLIA regulations to ensure laboratories meet general cybersecurity standards.
- A member commented that differing regulations on using cloud-based systems and cybersecurity measures across federal, state, and local jurisdictions pose challenges when recommending a universal standard, as some laboratories or jurisdictions may struggle to comply.
- Another member suggested providing educational resources describing the cybersecurity risks related to laboratory testing and providing possible mitigation strategies or plans to assist smaller organizations that may not have access to services offered by larger healthcare institutions.
- A CLIAC member questioned whether the CLIA regulations should focus on downtime procedures that may result from a cybersecurity attack, suggesting that specific language on cybersecurity should be included in CLIA. The member emphasized the need for alignment between the requirements of the accreditation organizations such as the Joint Commission and the College for American Pathologists for hospitals and those of CLIA for laboratories and proposed that recommendations should focus on integrating these guidelines to ensure a cohesive approach to cybersecurity across hospital systems. Several members agreed that a continuity of operations plan in the event of a cybersecurity attack should be required under CLIA.
- Several members emphasized the need for clear but non-duplicative cybersecurity guidance for laboratories, drawing on established frameworks like the National Institute of Standards and Technology (NIST) recommendations referenced by the Health Insurance Portability and Accountability Act (HIPAA).
- One member expressed concerns about overburdening laboratories with requirements beyond their capacity, especially smaller laboratories lacking IT resources. Another member indicated that the focus should be on providing practical support to laboratories without imposing unnecessary or redundant regulations.

Committee Recommendations

The Committee deliberated, voted, and approved the following recommendations based on the topic of *Cybersecurity Requirements in the Clinical Laboratory*.

Recommendation 9: CLIAC recommends a regulation that requires laboratories to have a documented cybersecurity plan. This includes defining what cybersecurity means for the clinical laboratory. CDC should create educational tools and resources for laboratories related to developing a cybersecurity plan.

Recommendation 10: CLIAC recommends updating the existing CLIA regulations to reflect modern cybersecurity and information management issues.

Proficiency Testing: Determination of Clinically Relevant Range of Values

Introduction to Topic

Angelique Daubert, MLS(ASCP)
Branch Manager, Regulations and Clearance Branch
Division of Clinical Laboratory Improvement and Quality
Quality, Safety, and Oversight Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services

Víctor R. De Jesús, PhD
Acting Director, Division of Laboratory Systems
Director, Quality and Safety Systems Branch
Office of Laboratory Systems and Response
Centers for Disease Control and Prevention
Presentation 9

Ms. Daubert provided an overview of the approval process for proficiency testing (PT) programs, including the collaboration between CMS and CDC, to evaluate these programs before approval. She noted that CMS assesses program administration and the PT proposed content, while CDC analyzes data from the previous year's offerings to ensure compliance with the CLIA regulations. Ms. Daubert asked the Committee to focus on PT program requirements, which mandated that annual programs provide samples representing a full range of patient specimens across various categories, including syphilis serology, routine chemistry, toxicology, hematology, and immunohematology. She emphasized that a significant challenge for PT programs was supplying samples at the lower end of the range due to complexities involving multiple instruments and analytes. Dr. De Jesús explained the CDC's methods to analyze the PT program's compliance with the CLIA requirements using available data and reference ranges. He noted that reference ranges from the Mayo Clinic test menu are primarily used but notes that five analytes are not included on this site and other options are utilized. Dr. De Jesús emphasized the need for more information about reference ranges to enhance the PT program analysis for approval.

Proficiency Testing: Measuring the Clinically Relevant Range of Values

Nikola A. Baumann, PhD
Vice Chair of Quality,
Co-Director, Central Clinical Laboratory, and Central Processing Laboratory
Director, Process Innovation through Automation (PITA) Laboratory,
Department of Laboratory Medicine and Pathology
Mayo Clinic
Presentation 10

Dr. Baumann provided an overview of clinically relevant ranges for laboratory assays, emphasizing their broader scope beyond reference intervals. She noted that reference intervals, typically the central 95th percentile of a healthy population, were described as method- and population-specific but not diagnostic of health or disease, noting that clinically relevant ranges encompassed medical decision limits, which guided therapeutic or diagnostic actions. Dr. Baumann provided case studies, TSH, free thyroxine (FT4), and serum glucose to illustrate how clinically relevant ranges extended beyond reference intervals, addressing both diagnostic thresholds and critical values. She highlighted that changes in laboratory results over time (delta values) are pivotal for monitoring physiological changes and treatment responses. She noted that analytical considerations ensured precision and accuracy across the measurement range, including clinically irrelevant values. Dr. Baumann proposed framing the Committee discussion by identifying clinically irrelevant ranges, which highlighted extreme values while maintaining laboratory accountability, and suggested that a data-driven approach that integrated reference intervals, therapeutic thresholds, and patient trends offered a more robust understanding of clinical relevance.

Public Comments

PC2: The College of American Pathologists (CAP)
PC3: The American Proficiency Institute (API)

Committee Discussion

- The CLIAC Chair emphasized the importance of defining clinically relevant ranges or potential targets for PT (proficiency testing) programs beyond the current requirements and suggested that PT programs should include events at clinical or medical decision points in addition to low and high extremes to highlight the importance of incorporating critical values into PT programs to reflect treatment decision thresholds.
- A CLIAC Member expressed confusion about how PT could address deltas (changes over time), which are crucial in clinical practice but not currently reflected in PT program content. The member raised concerns about dynamically determined patient reference intervals and questioned how these could be integrated into future PT frameworks. They also acknowledged the artificiality of static reference ranges when applied to individuals. In response, the CLIAC Chair agreed on the importance of deltas for patient care but noted that PT programs are static assessments, making it challenging to incorporate delta values.
- A member discussed the difficulties varying reference ranges pose across organizations and platforms.
- One member proposed that PT program providers should identify medical decision points, supported by literature, for evaluation by the PT program and suggested that PT cycles include testing within 10% of either the upper or lower medical decision limits at least once over the course of a cycle.
- Multiple Committee members were concerned about how PT programs could utilize medical decision points, as many decision points are based on the patient population of the testing laboratory.
- Multiple members questioned and discussed the feasibility of medical decision points when many manufacturers and methods use the PT materials, and the methods typically have different reference ranges for the same analytes. Several members added that many decision points are based on the patient population of the testing laboratory, and using medical decision points may not be logistically feasible as it would result in personalization of PT programs based on the institution.
- A Committee member suggested that PT should be kept analytical performance and not use medical decision points. Another Committee member suggested finding a middle ground using a matrix rather than a statistical approach.
- A CLIAC member asked if there was a way to account for results when a proficiency testing sample was run on different instruments. Another member answered that in PT, the information is analyzed by a peer group, which accounts for some of the variation in the test systems.
- Another committee member commented that PT programs should test the full analytical measurement range (AMR), and the AMR should be enough, especially as it often falls near or at medical decision points.

Committee Recommendations

The Committee deliberated, voted, and approved the following recommendations based on the topic of *Proficiency Testing: Determination of Clinically Relevant Range of Values*.

Recommendation 11: CLIAC recommends that the CLIA requirements for proficiency testing programs be updated to include consideration for analytical measurement ranges, including those values that may be medically relevant, if possible, for regulated analytes.

Utilization of Remote Technology for Competency Assessments

Introduction to Topic

Gregg S. Brandush, RN, JD
Director
Division of Clinical Laboratory Improvement and Quality
Quality, Safety, and Oversight Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
Presentation 11

Mr. Brandush introduced the session by discussing the longstanding debate surrounding virtual competency assessments in clinical laboratories, which has been explored in various forms over the years. He shared insights from a recent poll, which found significant opposition to virtual assessments among state agencies,

CMS locations, and accrediting organizations, primarily due to concerns over maintaining the highest standards of competency evaluation. Despite this resistance, Mr. Brandush emphasized the importance of considering emerging technologies that could improve assessment quality and reduce costs. He asked the committee for feedback on whether CLIAC should recommend greater regulatory flexibility for virtual competency assessments in laboratories, considering factors such as the potential loss of competency compared to in-person observations, appropriate limits on virtual assessments, required technology guidelines, workload limits, and possible regulatory changes for technical supervisors and consultants.

Leveraging Technology for Remote Assessments

Ms. Michele Klawitter
Vice President
Quality Systems
American Red Cross

Ms. Andrea Noon
Director
Training Strategy
American Red Cross

Mr. Richard Redman
Practice Leader
Human Capital Initiatives
Computer Generated Solutions
Presentation 12

Ms. Klawitter and Ms. Noon shared their experience integrating wearable technology into competency assessments as part of their efforts to modernize training programs. Mr. Redman then explained how the Realwear Navigator 520 wearable device allows staff to complete assessments hands-free while providing direct, secure observation through first-person video. He discussed how technology, specifically the Realwear Navigator 520, could enhance training and competency assessments. He noted that the device allows hands-free operation with voice recognition and is compatible with personal protective equipment (PPE). Ms. Noon highlighted several key advantages of the technology, such as increased flexibility, reduced travel, and minimal disruption. She also noted that the device improves assessors' visibility, enabling them to zoom in on specific details. Lastly, Ms. Noon shared results from a mock assessment using the Realwear device, noting that participants found it practical or more effective than traditional methods. She noted that feedback indicated that the first-person viewpoint provided by the device enhanced visibility during assessments. Ms. Klawitter concluded by discussing potential risks associated with introducing new technology into processes but assured that quality assurance measures were integrated into program development. She acknowledged concerns regarding connectivity issues and confirmed that in-person assessments would remain an option if needed.

Public Comments

PC 4: The College of American Pathologists (CAP)
PC 5: The American Association for Laboratory Accreditation (A2LA)

Committee Discussion

- Many CLIAC members expressed enthusiasm about integrating wearable technology into competency assessments while emphasizing its potential benefits for improving training outcomes and operational efficiency.
- Several members raised concerns about misidentifying individuals and security issues with protected health information, but the group felt these risks were manageable through existing regulations and technology.
- Members did not deem any laboratory subspecialty entirely unsuitable for remote assessment, though one member noted microscopy as a potential challenge due to current technology limitations.
- Several members emphasized that remote competency assessments should be conducted one-on-one, especially during the early stages.
- Several CLIAC members suggested remote assessments could be broadened to include third-party assessors for specialized areas (e.g., molecular testing), while others preferred that site supervisors familiar with the local environment and protocols remain the primary assessors.

- Multiple Committee members agreed that remote assessments could lead to a more flexible and expansive competency model, potentially incorporating virtual and augmented reality technologies for training and assessments.

Committee Recommendations

The Committee deliberated, voted, and approved the following recommendations based on the topic of the *Utilization of Remote Technology for Competency Assessments*.

Recommendation 12: CLIAC recommends that CMS allow remote assessment to be utilized in the direct observation component of competency assessment.

CLOSING REMARKS/ADJOURN

Dr. Laser and Ms. Stang expressed gratitude to the CLIAC members for their engagement and excellent discussion and acknowledged the staff who assembled and organized the meeting agenda. Dr. Laser reminded members of the April 9-10, 2025 meeting and indicated that agenda topics can be sent to CLIAC@cdc.gov. With no further business posed or questions/comments raised, the meeting was officially adjourned.

CERTIFICATION

I hereby certify that, to the best of my knowledge and ability, the foregoing minutes of the November 6-7, 2024*, Clinical Laboratory Improvement Advisory Committee is* accurate and complete.

_____
Date

_____
Jordan Laser, MD
Chair, Clinical Laboratory Improvement Advisory Committee (CLIAC)
Centers for Disease Control and Prevention

CLIAC NOVEMBER 2024 AGENDA

Addendum 1

CLIAC NOVEMBER 2024 PRESENTATIONS

Addendum 2

CLIAC NOVEMBER 2024 PUBLIC COMMENTS

Addendum 3

CLIAC MEETING TRANSCRIPT

Addendum 4

Addendum 1

THE CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC)

Virtual Zoom Webinar

November 6, 2024

Time (EST)	Topic		Speaker/Moderator
11:00	Call to Order and Welcome		Dr. Jordan Laser Dr. Ren Salerno Ms. Heather Stang
	Recognition of New Members: • Ms. Heather Stang, CLIAC Designated Federal Officer • Dr. Víctor R. De Jesús, CDC Ex Officio • Dr. Olga Cerón • Dr. Soojin Jun • Dr. Anthony Tran		
	Recognition of Outgoing Member Ms. Heather Duncan	**1**	
11:10	Introductions and Conflict of Interest		Ms. Heather Stang
11:20	CDC Update	**2**	Dr. Víctor R. De Jesús
11:50	CMS Update	**3**	Mr. Gregg Brandush
12:20	FDA Update	**4**	Dr. Courtney Lias
12:50	**BREAK (one hour)**		
	CLIAC Workgroup Reports		
1:50	CLIAC Biosafety Workgroup Report	**5** **5a**	Dr. Michael Pentella
2:10	Public Comments		
2:15	Committee Discussion		Dr. Jordan Laser
3:15	**BREAK (15 minutes)**		
3:30	CLIAC NGS Workgroup Report	**6** **6a**	Dr. Nirali Patel
3:50	Public Comments		
3:55	Committee Discussion		Dr. Jordan Laser
5:00	Adjourn		Dr. Jordan Laser

THE CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE

Virtual Zoom Webinar

November 7, 2024

Time (EST)	Topic		Speaker/Moderator
11:00	Call to Order		Ms. Heather Stang Dr. Jordan Laser
	Cybersecurity Requirements in the Clinical Laboratory		
11:05	Introduction to the Topic	**7**	Mr. Gregg Brandush
11:15	Cybersecurity Considerations for Clinical Laboratories	**8**	Dr. David McClintock
11:35	Public Comments		
11:40	Committee Discussion		Dr. Jordan Laser
	Proficiency Testing: Determination of Clinically Relevant Range of Values		
12:40	Introduction to the Topic	**9**	Ms. Angelique Daubert Dr. Víctor R. De Jesús
12:50	Proficiency Testing: Measuring the Clinically Relevant Range of Values	**10**	Dr. Nikola Baumann
1:10	Public Comments		
1:15	Committee Discussion		Dr. Jordan Laser
2:15	**BREAK (1 hour)**		
	Utilization of Remote Technology for Competency Assessments		
3:15	Introduction to the Topic	**11**	Mr. Gregg Brandush
3:20	Leveraging Technology for Remote Assessments	**12**	Ms. Michele Klawitter Ms. Andrea Noon Mr. Richard Redman
3:50	Public Comments		
3:55	Committee Discussion		Dr. Jordan Laser
4:55	Meeting Wrap-up		
5:00	Adjourn		Dr. Jordan Laser

Addendum 2

Clinical Laboratory Improvement Advisory Committee

Meeting Presentations

November 6-7, 2024

Atlanta, Georgia

Division of Laboratory Systems

CLIAC Outgoing Member Recognition

Heather L. Stang, MS, MT
Senior Advisor for Clinical Laboratories
Division of Laboratory Systems
Office of Laboratory Systems and Response
CLIAC Designated Federal Officer

Heather Duncan, MPH, MT(ASCP), CQA(ASQ)

Ms. Duncan's diverse experience in industrial food safety, clinical laboratory testing, laboratory medicine, regulatory compliance, and quality assurance provided a diverse perspective to many CLIAC discussions. She was instrumental in leading recommendations related to the expansion of point-of-care testing during the COVID-19 pandemic, the future of laboratory medicine in non-traditional testing sites, efforts to address public health and clinical laboratory workforce challenges, the laboratory's role in advancing health equity, and efforts to address the CLIA top 10 laboratory deficiencies. Ms. Duncan served as the Chair of the CLIAC CLIA Certificate of Waiver and Certificate for Provider-performed Microscopy Workgroup and as a member of the CLIAC Biosafety Workgroup. We thank Ms. Duncan for her commitment to the Committee.

Division of Laboratory Systems

CDC Update

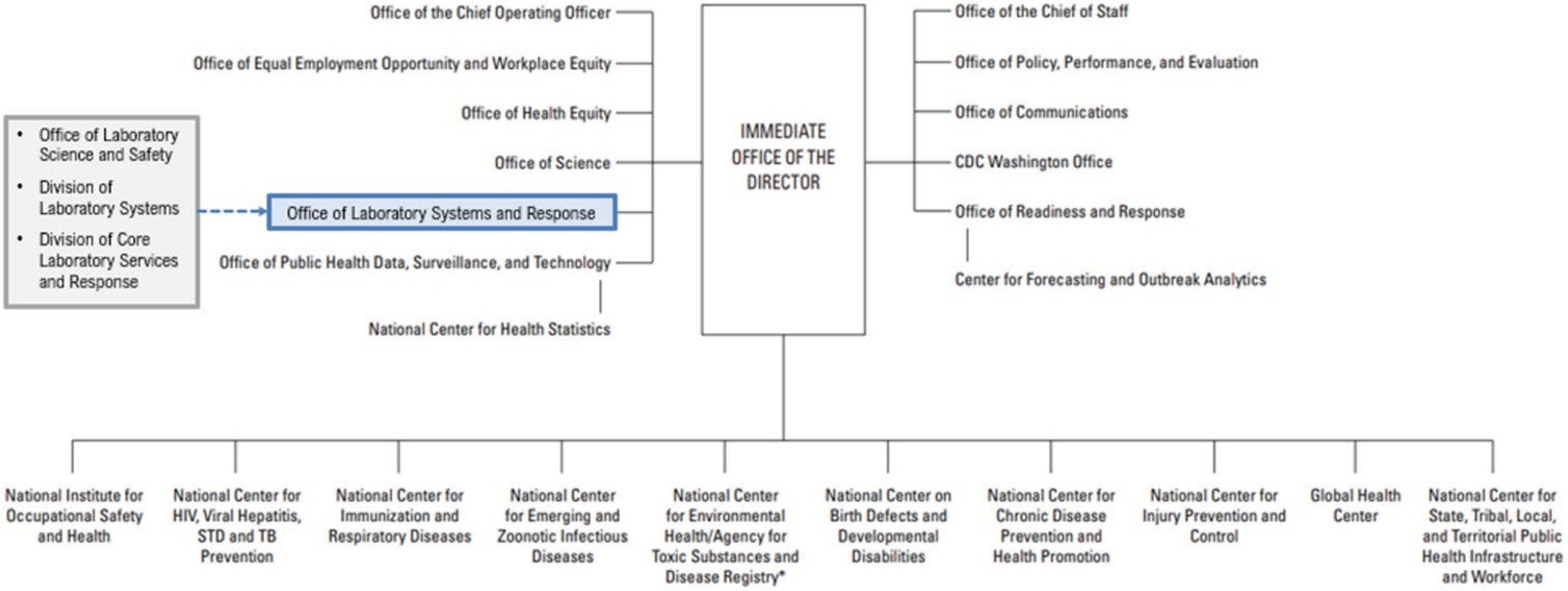
Víctor R. De Jesús, PhD
Acting Director
Division of Laboratory Systems
Office of Laboratory Systems and Response

CLIAC Fall Meeting 2024

ONE CDC:
OLSR REALIGNMENT

Department of Health and Human Services

Centers for Disease Control and Prevention (CDC)



*ATSDR is an OPDIV within DHHS but is managed by a common director's office.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

Office of Laboratory Systems and Response (OLSR)

Mission

Create a core laboratory infrastructure that provides operational and systems support to CDC and the nation's public health and clinical laboratories, ensuring

- High-quality and safe laboratory science
- Reliable diagnostics for outbreaks and harmful exposures
- Improved laboratory readiness and response

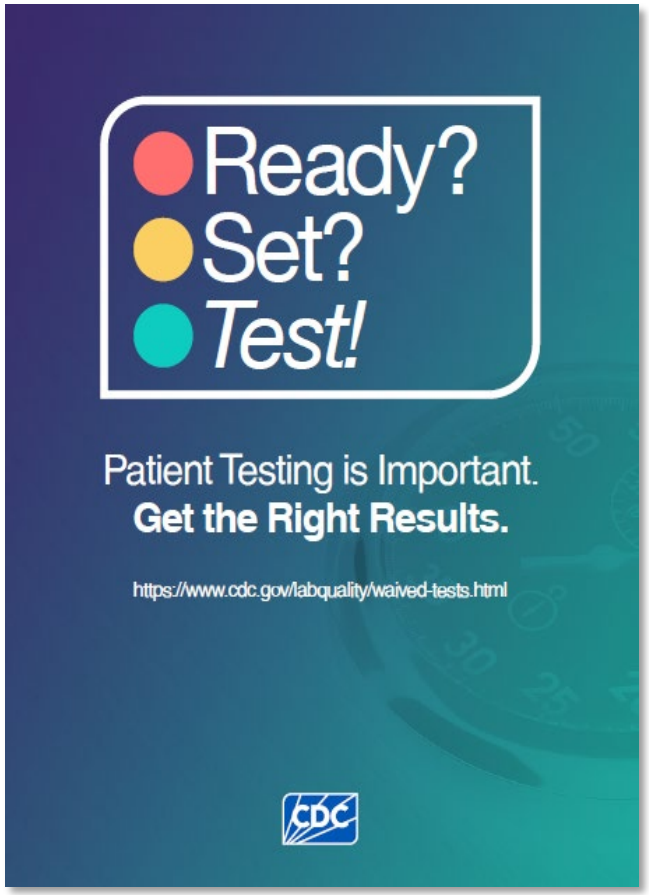
LABORATORY QUALITY

Waived Testing Educational Material Updates

Ready? Set? Test!

- ***New!* Design and Considerations for Performing Waived Tests**
  - Updated CLIA guidelines – PT Referral for Certificate of Waiver sites
  - Updated safety guidance
  - Quality assessment practices
  - Self-Assessment Checklist for Good Testing Practices
- **Impact**
  - Over **1,300 physical booklets** were distributed to the laboratory community this year!
  - Over **1,000 booklets** were downloaded in FY 2024!

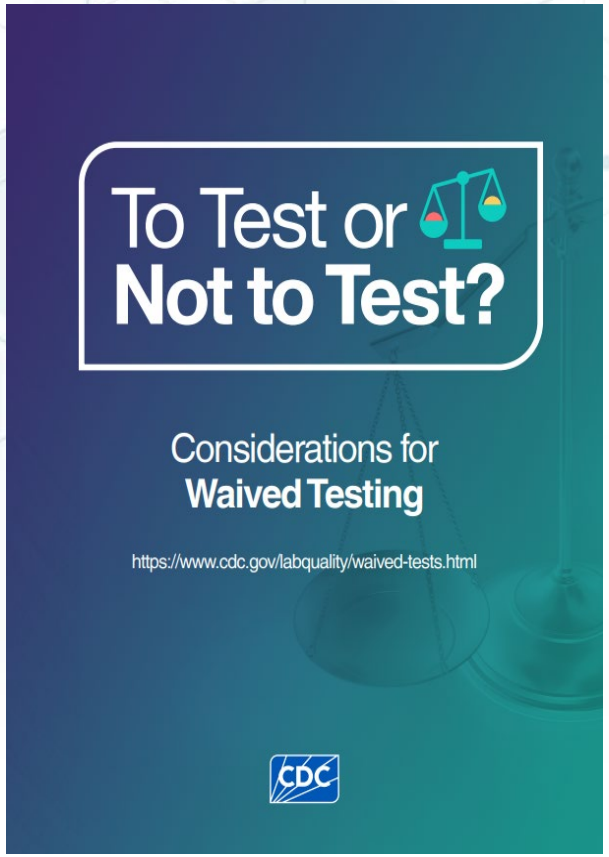
https://www.cdc.gov/lab-quality/php/waived-tests/index.html



Spanish version coming soon!

Waived Testing Educational Material Updates

To Test or Not to Test?



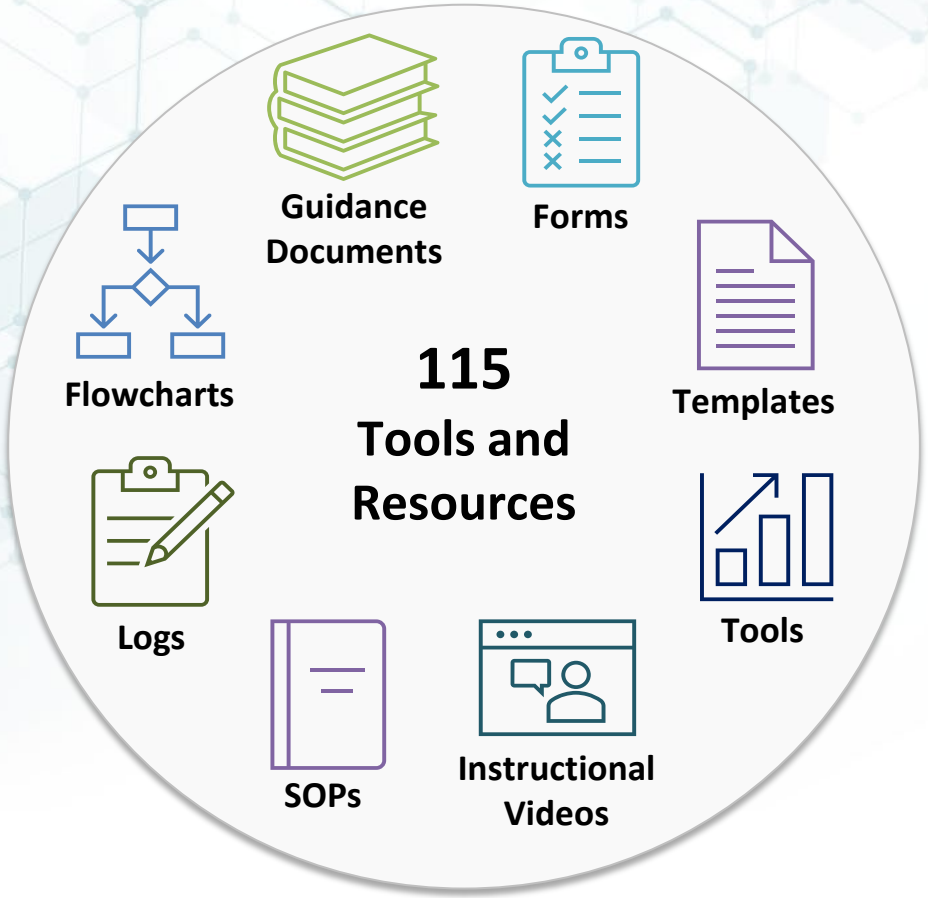
Spanish version coming soon!

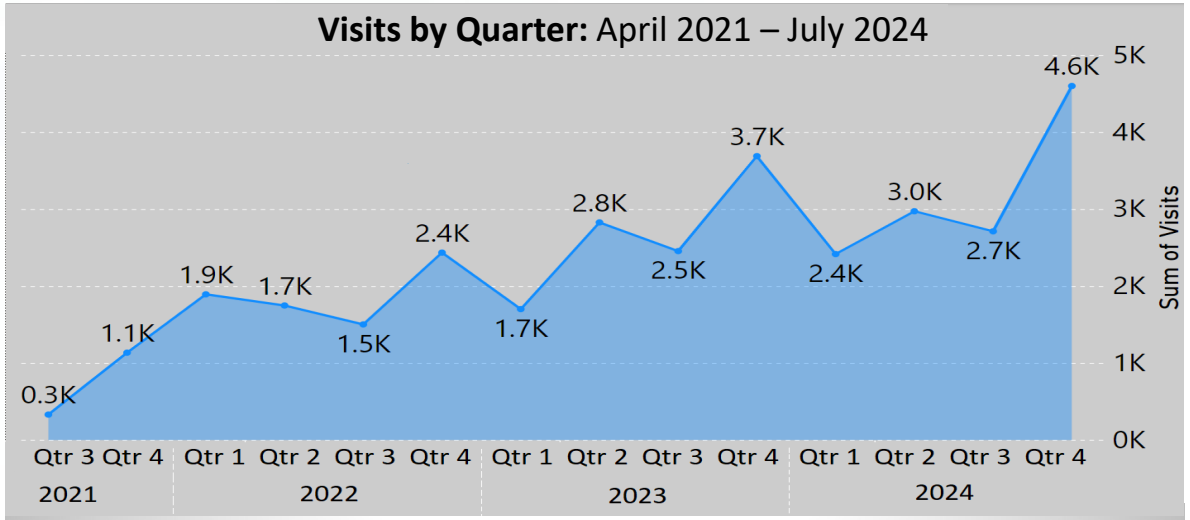
- ***New!* Design and Considerations for Performing Waived Tests**
  - Updated CLIA Certificate of Waiver Requirements for multi-location testing sites
  - Updated CLIA guidelines – PT Referral for Certificate of Waiver sites
  - General safety considerations
- **Impact**
  - Over **600 physical booklets** distributed to the laboratory community this year!
  - Over **1,300 booklets** downloaded during FY 2024!

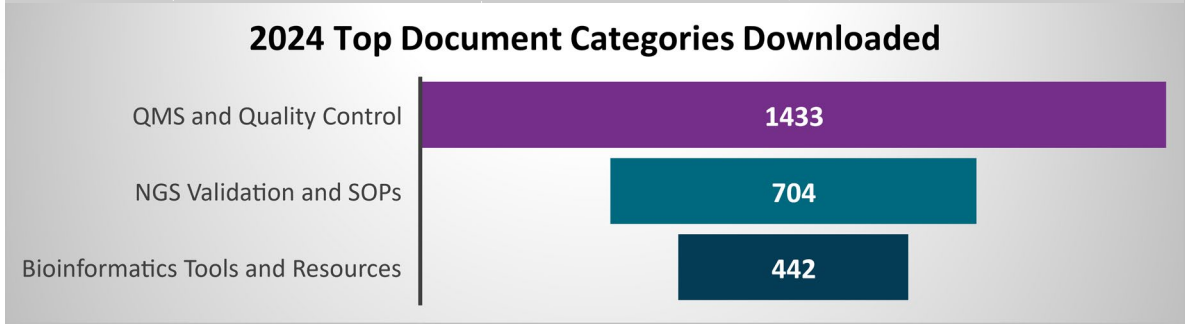
https://www.cdc.gov/lab-quality/php/waived-tests/index.html

Next Generation Sequencing Quality Initiative

Tools and Resources





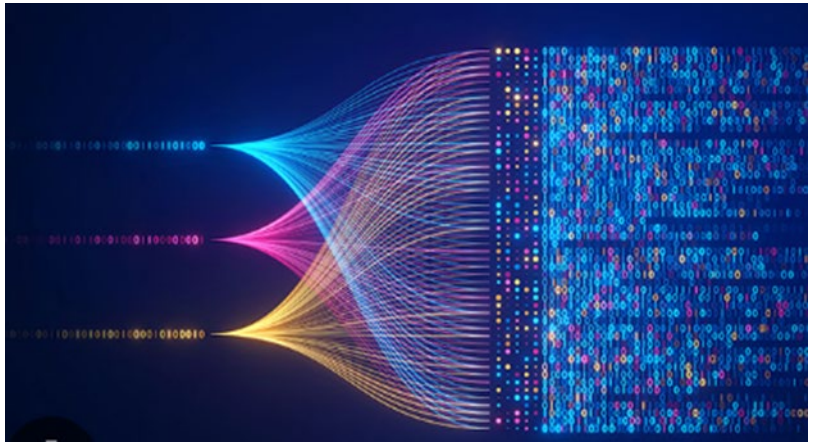


https://www.cdc.gov/lab-quality/php/ngs-quality-initiative/qms-tools-resources.html

Next Generation Sequencing Quality Initiative

Meeting the Needs of the Sequencing Community

- QMS Assessment Tool Update
- Pathway to Quality-Focused Testing: https://www.cdc.gov/lab-quality/php/pathway/pathway-to-testing.html
- Reference Materials
- Automated end-to-end sequencing platforms

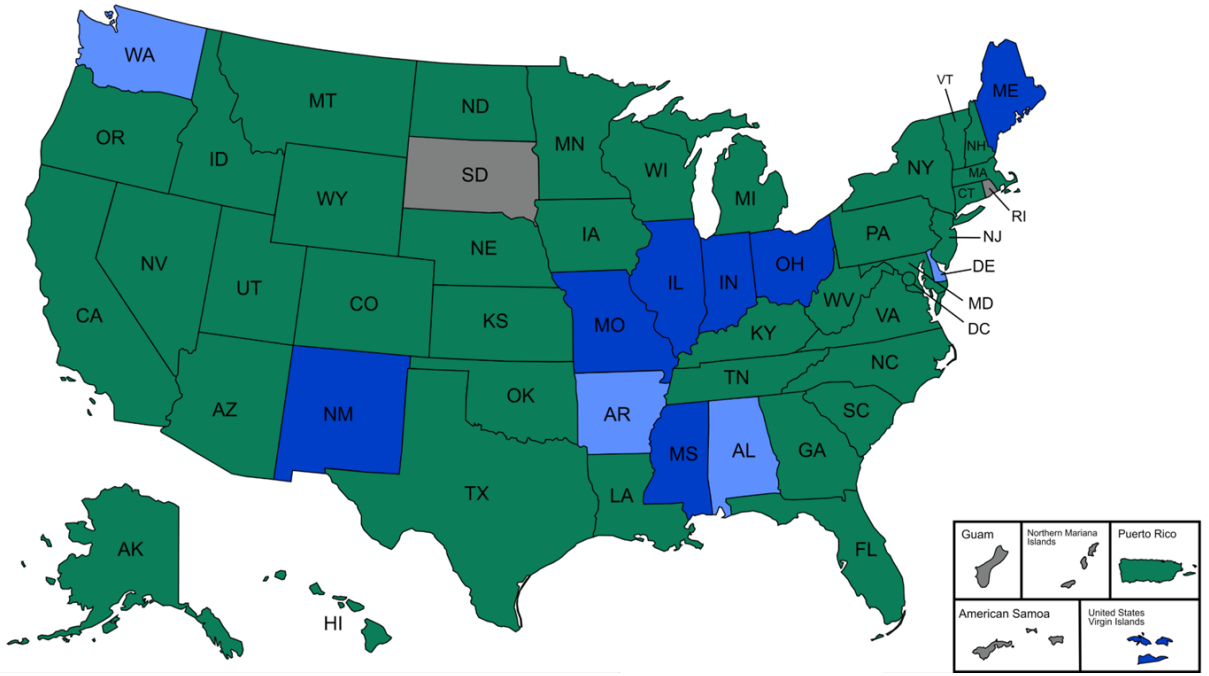


LABORATORY SAFETY

ECHO Biosafety Program

524 participants attended the session

219 organizations were represented



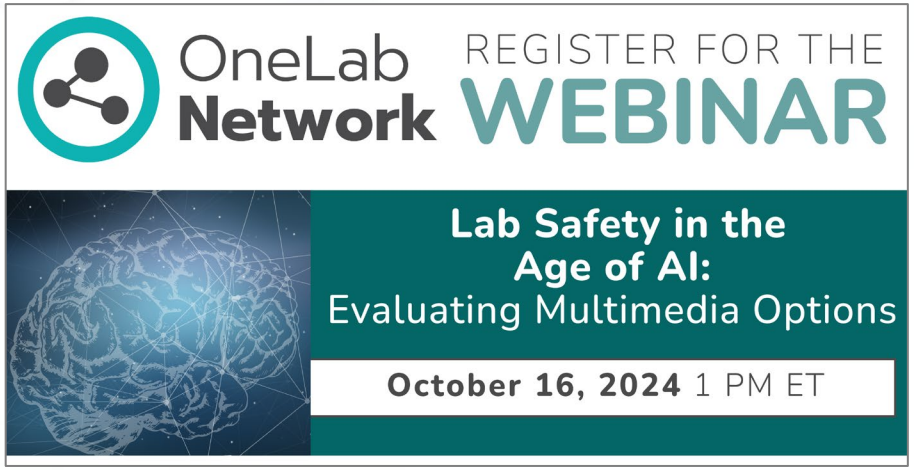
Note: Participants from Belize, Canada, El Salvador, India, Indonesia, and Italy also attended sessions.

Upcoming Sessions

- **November 19:** Biorisk Management Performance Evaluation
- **December 17:** Biorisk Management Improvement

https://www.cdc.gov/safe-labs/php/echo-biosafety/

Biosafety and Biosecurity Month

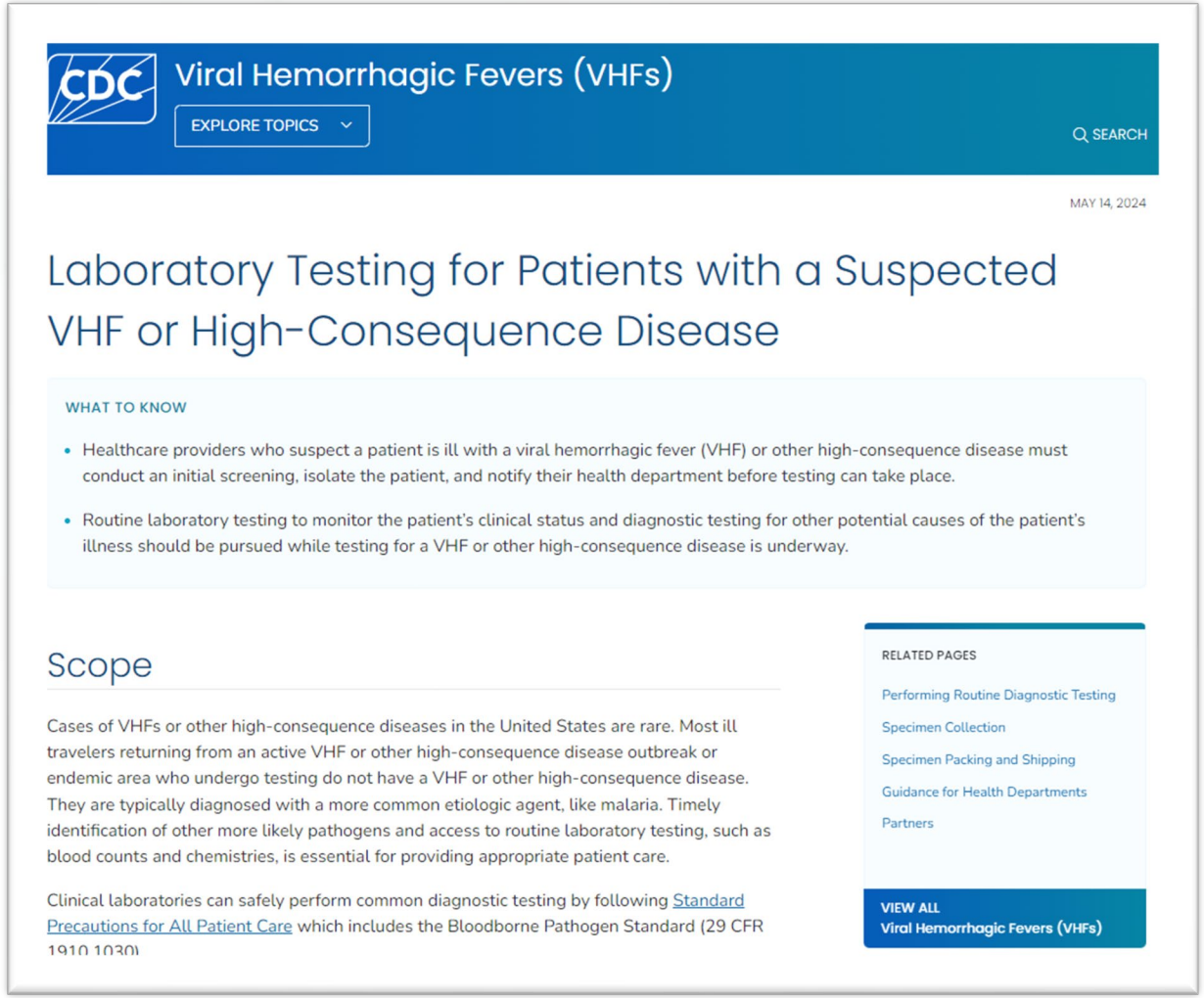


https://www.cdc.gov/safe-labs/php/about/

Viral Hemorrhagic Fever

CDC Guidance Revisions

- Select Viral Hemorrhagic Fevers
- Viral hemorrhagic fevers are in risk group 4
- BSL-4 facilities are recommended for viral propagation and research activities (BMBL)
- Clinical laboratories have different requirements due to smaller contained specimens that could contain unknown pathogens (BMBL Appendix 4)
- Comprehensive updates have been made to VHF pages



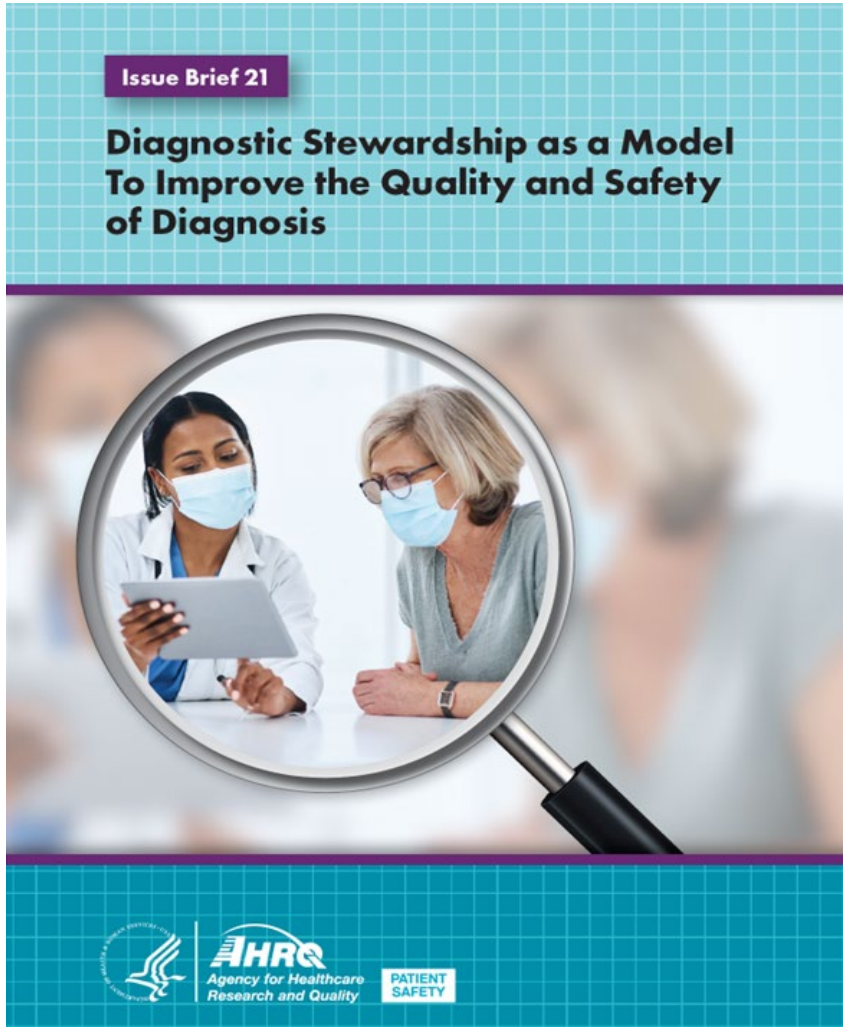
DIAGNOSTIC EXCELLENCE

Diagnostic Excellence

- Issue Brief - Diagnostic Stewardship as a Model to Improve the Quality and Safety of Diagnosis, August 2024; in collaboration with the Agency for Healthcare Research and Quality

- Core Elements of Hospital Diagnostic Excellence, September 2024; in collaboration with the CDC Division of Healthcare Quality Promotion

- Why Clinical Laboratory Testing Matters
  - Patient-directed educational resource about the total testing process, using early diagnosis for chronic kidney disease as a model
  - Release date – 4th quarter 2024



BD Blood Culture Bottle Shortage

Collaboration between CDC, FDA, CMS, and IDSA

July-October

- **Communication and strategies developed to assist clinical laboratories**
  - Outreach through LOCS, CDC/IDSA webinars, HANs messaging, and BD website
- **Provided Diagnostic Stewardship guidance on:**
  - Reducing blood culture (BC) contamination (lowers the need for additional BC)
  - On monitoring correct volume drawn on initial request (lowers the need for additional BC)
  - Evidence-based strategies to improve inpatient blood culture utilization: 25 to 60% of BC may be unnecessary

- Fabre V, et al . A Diagnostic Stewardship Intervention To Improve Blood Culture Use among Adult Nonneutropenic Inpatients: the DISTRIBUTE Study. J Clin Microbiol. 2020.

LABORATORY READINESS AND RESPONSE

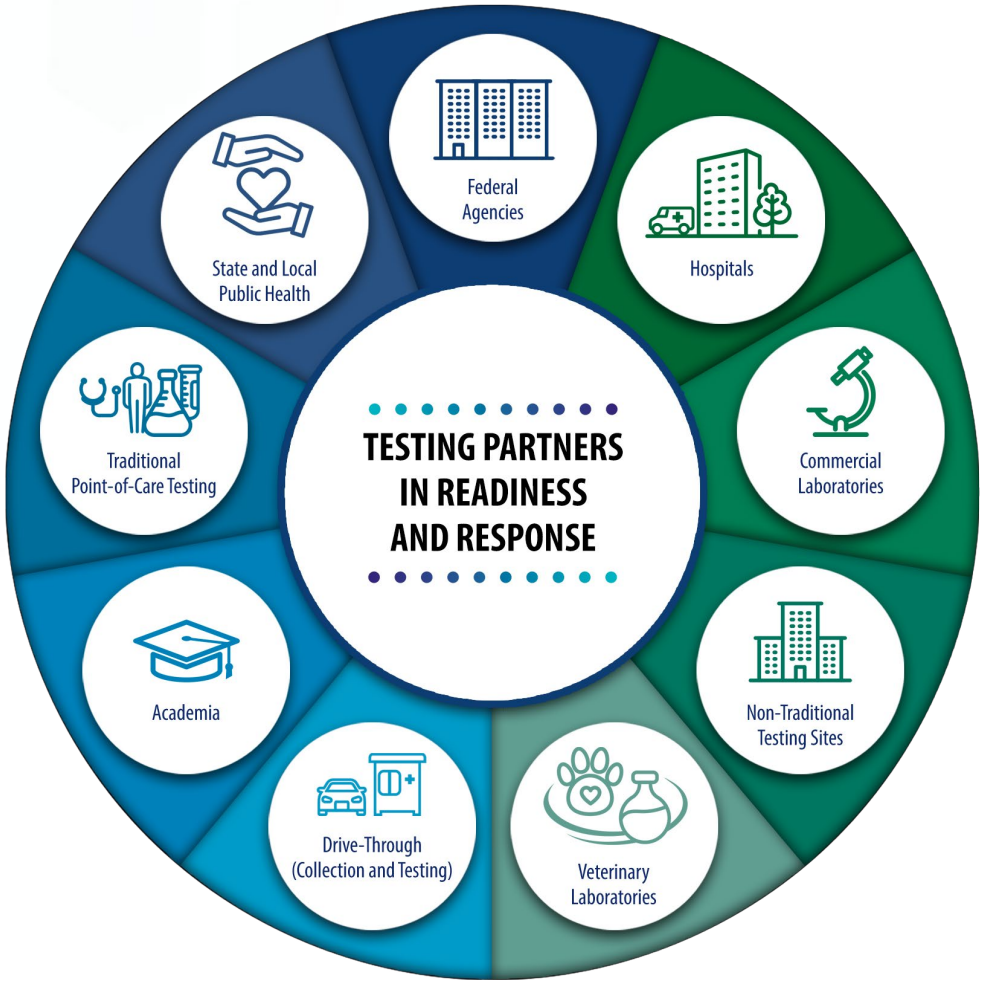
Laboratory Response Network for Biological Threats

- The LRN-B is celebrating its 25th anniversary in 2024
- In 2024, the LRN-B supported CDC's success in obtaining updated EUAs for mpox and MERS
- Collaborating to ensure LRN testing data is widely available for CDC use

https://emergency.cdc.gov/lrn/biological.asp

Clinical Laboratory Engagement Team Activities

- **National Response Testing Framework**
  - Roadmap for surge testing support
  - Building testing capacity with commercial laboratories
- **MOU for Surge Testing**
  - Membership expansion
- **Emergency Responses**
  - Mpox
  - Influenza H5
  - VHFs
- **Laboratory Outreach Communication System (LOCS)**
  - 39 messages and 9 calls



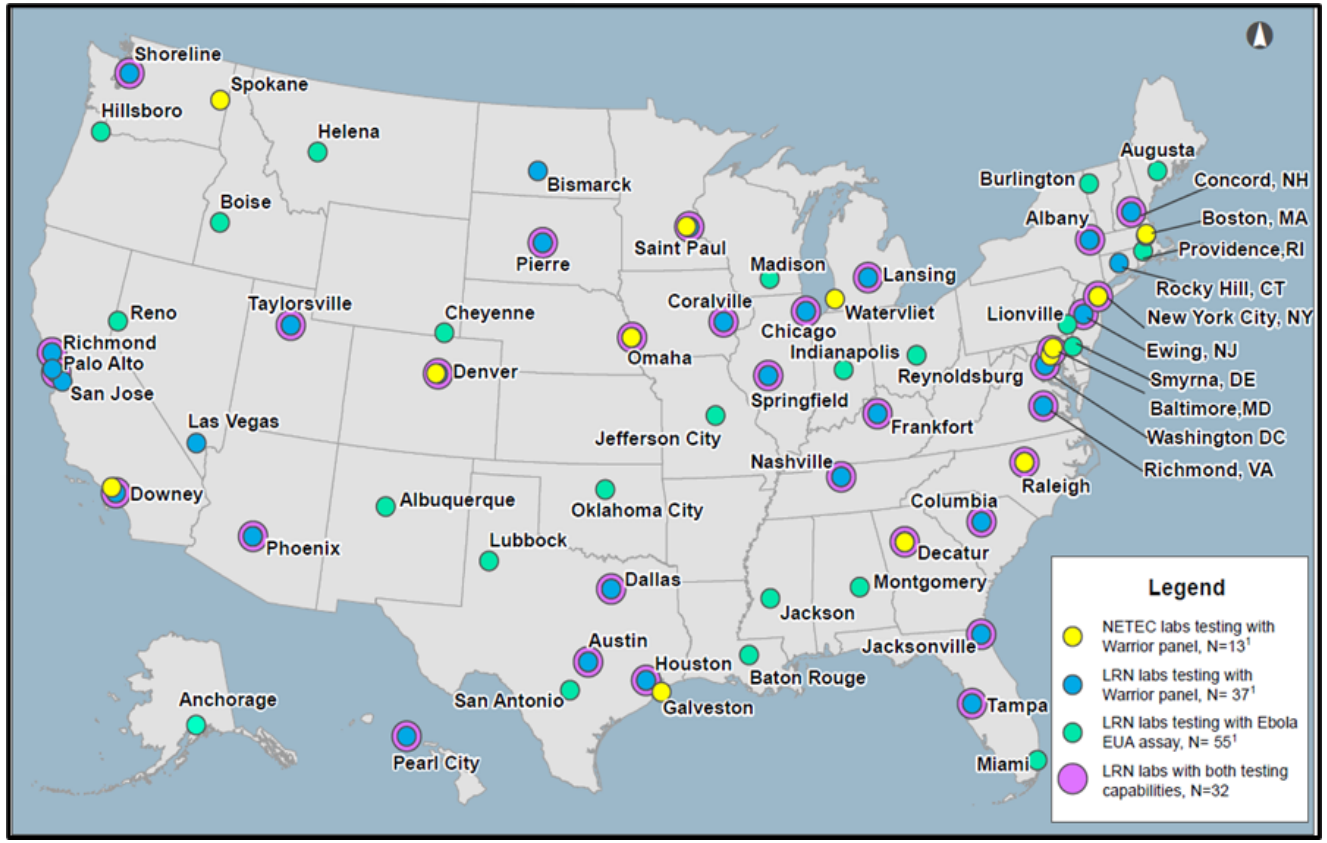
Surge Testing, Test Development, and Data Sharing Indefinite Delivery Indefinite Quantity (IDIQ) Contract

- CDC recently awarded a contract to Labcorp, Aegis, ARUP, Quest, and Gingko Bioworks
- Warm base capacity, surge diagnostic testing, test development, and specimen collection
- Data sharing for over 200 reportable conditions

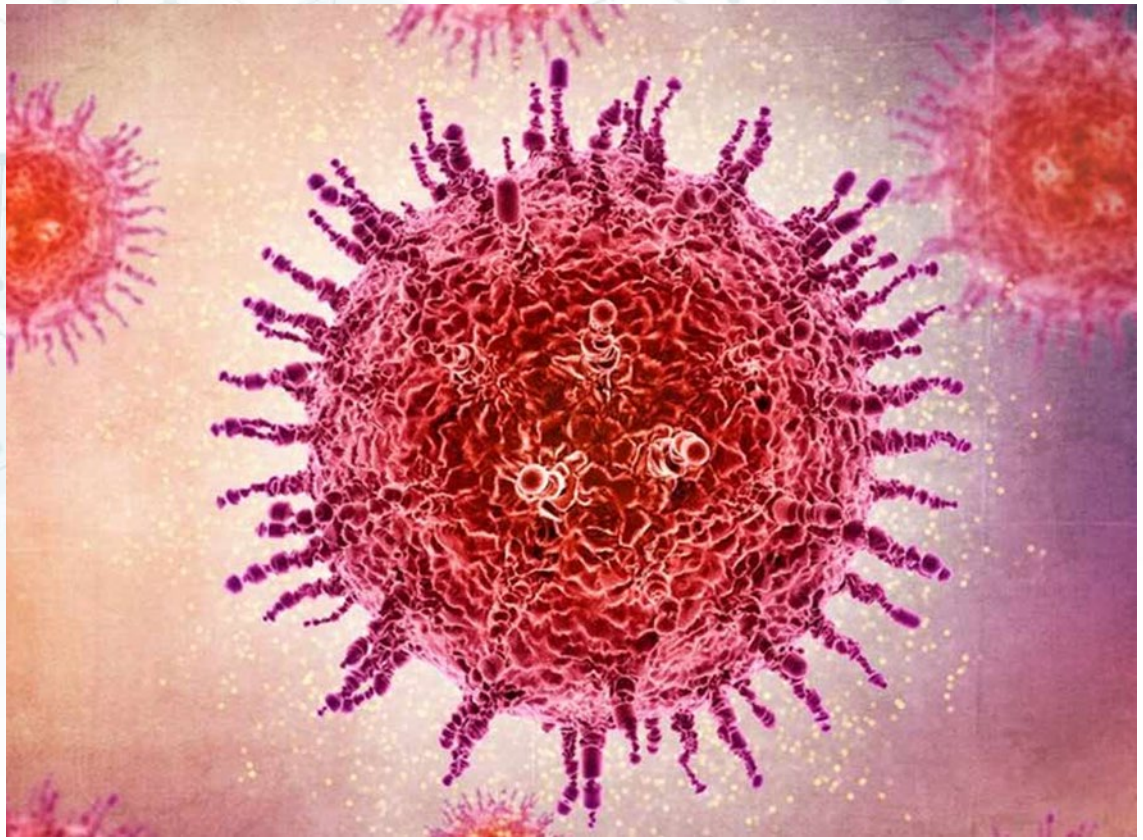
Resource: Strengthening Response to Public Health Threats through Expanded Laboratory Testing and Access to Data (cdc.gov)

Marburg 2024 Response

- Rwanda is experiencing its first Marburg outbreak
- 6 cases, most are healthcare workers and their contacts link to two hospitals
- CDC and 40 Laboratory Response Network (LRN) laboratories have testing capability



Oropouche



- More than 8,000 cases reported from South America and Cuba
- Approximately 20 cases in travelers returning to US
- CDC currently has CLIA PRNT and RT-PCR tests (Fort Collins)
- RFP for Oropouche test development in process (IDIQ)

LABORATORY TRAINING: ONELAB™ INITIATIVE

OneLab Initiative

OneLab™ membership has **doubled** since April 2024, now totaling over **41,000 unique members**!

OneLab Resources

- OneLab training materials (eLearning and VR courses, job aids, webinars, videos, etc.) attracted **439,000+ registrations** in FY24 – 2.6 times the FY23 total
- Launched new eLearning courses in Fall 2024:
  - *Fundamentals of Quality Management Systems*
  - *Fundamentals of Bloodborne Pathogens*
- Just launched: OneLab VR Autoclave Safety

OneLab REACH™ — **38,900+ learners** with **18,900 new learners** in the past six months

OneLab Network — **18,000+ members** with **8,300 new members** in the past six months

OneLab TEST — **8,000+ members** with **4,300 new members** in the past six months

https://www.cdc.gov/lab-training/php/onelab

CLIA Laboratory Director University (LDU)

- CMS and CDC are partnering to develop a free, online training program to meet CLIA's continuing medical education (CME) requirement for doctors of medicine, osteopathy, or podiatric medicine seeking to qualify to direct a laboratory that performs moderate complexity testing
  - 20+ hours of CME credits
  - Combination of webinars, eLearning courses, job aids, case studies, and other training formats with pre/post tests and a capstone to assess knowledge gain
  - Online CLIA surveyor tool will map training materials to common deficiencies so that they can serve as initial remediation as appropriate
  - Will include an evaluation of LDU's short-term and long-term impact

LDU Trainings in Development

- CMS approved the overall training plan in March 2024
- Three eLearning courses launching between late 2024 and mid 2025:
  - CLIA Proficiency Testing
  - CLIA Personnel Qualifications and Responsibilities: High Complexity Testing
  - CLIA Personnel Qualifications and Responsibilities: Moderate Complexity Testing
- Based on CMS feedback, CDC/DLS is developing the outlines for the remaining trainings and will send them in batches for CMS review
- Goal: To launch all trainings and the online tool for surveyors by 2027

DATA SCIENCE

Systemic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD) Workgroups

Data Exchange Standards

- **Define Standards** that enable reliable semantic interoperability and data exchange
- Ensure **consistent data flow** throughout the healthcare system

Create Knowledge Management Tools

- **Laboratory Interoperability Device Reference (LIDR)** and infrastructure to harmonize test information
- **In Vitro Diagnostic (IVD) Data Hub** and associated tooling to access de-identified data

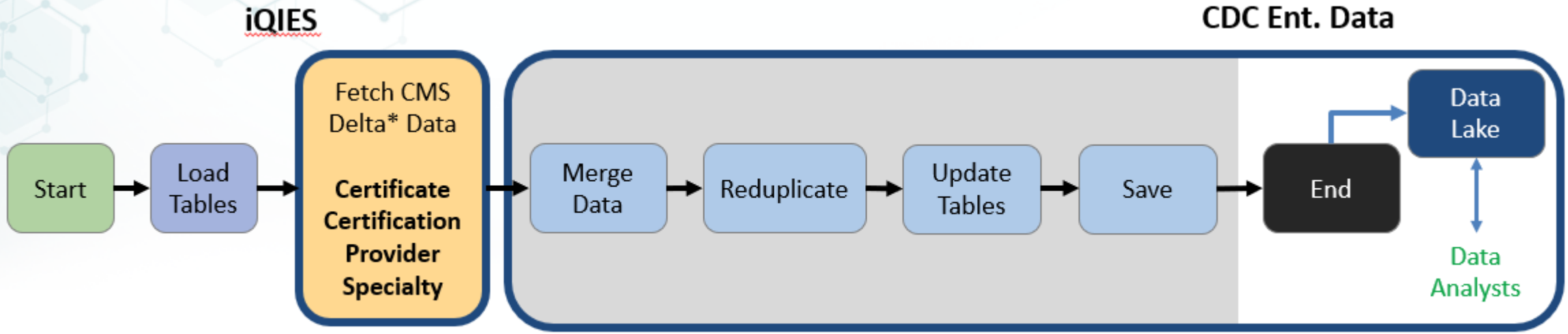
Communications

- **Communication and Branding** to align public and private partners on a single way forward

CMS to CDC Data Stream (C2CDS)

Modernizing Data Transmission

- Automated data transmission from the CMS Internet Quality Improvement & Evaluation System (iQIES) to CDC's enterprise data environment
- Consolidate multiple data sources into the CDC data lake
  - Accelerate access to & analysis of data



*Delta: All observations that have been modified since the data were last processed.

Exploring Laboratory-Led Interventions With Real-World Data

Commercially Available EHR and Claims Databases

- Use of Electronic Health Record (EHR) and medical claims data to explore use of laboratory-related data to improve patient care

Robust, Complex Data

- Medical history
- Diagnostic codes
- Medications

Representativeness

- >150 million patients
- Billions of patient encounters
- Inpatient and outpatient

- **Laboratory test data**
- Costs
- Demographic data
- Laboratory test result*

*Zhang et al. and Ehrenstein et al.

Real-World Data Examples

Guideline Recommended Pharmacogenetic Testing

Study to evaluate adherence to recommended genetic testing

- HLA-B*57:01 screening before abacavir prescription
  - screening supported by literature, guidelines, and an FDA black box warning
  - <50% of patients with HIV screened prior to drug initiation

Adult Blood Culture Contamination Rate

A national measure for clinical laboratories and antibiotic stewardship programs

- Utilizing EHR data in determining
  - sepsis testing accuracy
  - blood culture contamination rates

HEALTH EQUITY

Advancing Electronic Test Orders and Results (ETOR) to Promote Health Equity

What We'll Do

Goal: By December 2025, **30% of newly established ETOR systems** will be between public health laboratories and healthcare organizations that support people who are medically underserved.

Why It Matters

ETOR enables **direct exchange** of patient information, test orders, specimen data, and test results **improving data quality and timeliness**

What we have accomplished

Five jurisdictions are participating in an initial implementation of **ETOR for newborn screening**.

CDC and APHL are providing technical assistance **to the Iowa PHL and its partne healthcare organization in Alaska**, which serves **medically underserved areas and populations (MUA/Ps).**

Partners in Florida are exchanging ~500 orders and results a weel since they **launched ETOR in August** with results in the patient's chart **~2 days sooner**.

The **strategies, technologies, and partnerships** gained from the initial implementations can be used to **expand ETOR to other use-cases and to partners in MUA/Ps**.

Million Hearts Project

LDL Lab Messaging Project

- Designed to achieve timely diagnosis of severe hypercholesterolemia and statin prescribing to reduce risk for heart disease
- Implemented a process at Zufall Health, a federally qualified health center, to identify test results reporting LDL ≥ 190 mg/dL that triggers messaging to patients and their clinicians
- Increased statin prescribing found in preliminary analysis of results
- Mapped the workflow at Zufall Health as a basis to scale processes to other federally qualified health centers

Increasing Diversity within the Laboratory Workforce

Why It Matters

The public health laboratory workforce should **better reflect the diversity of the communities** it serves

COVID-19 highlighted **disparities in the public health laboratory workforce**

Reducing disparities hinges on expanding the workforce pipeline

What We'll Do

Identify barriers through feedback from organizations that serve under-represented groups (e.g., students of color, who are LGBTQ+, are veterans, have disabilities)

Reduce and eliminate barriers with continual partner input. **Attract more applicants from under-represented groups and communities** by increasing recruitment/promotion and ensuring selection criteria are clear and objective

How We'll Do It

Expand laboratory fellowships and internships program

Goal: By September 30, 2026, **increase the percentage of graduate fellows and undergraduate interns from under-represented groups and communities by 40%** placed in state, local, territorial public health laboratories

Leverages **new ARP investments**

Thank you!

vdejesus@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

CMS CLIA Update

Gregg Brandush

Division of Clinical Laboratory Improvement and Quality

November 6, 2024

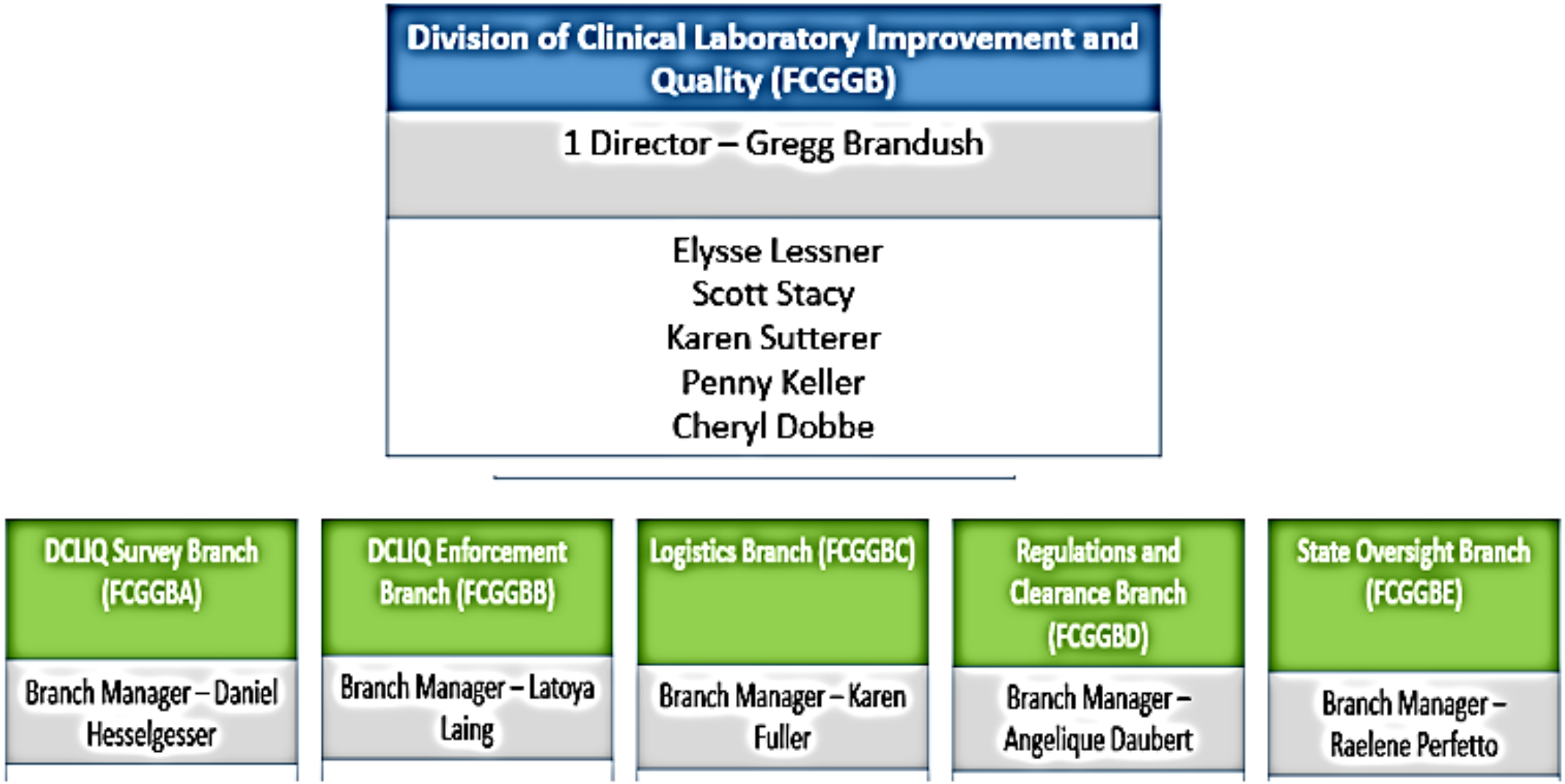
Disclaimer

- This presentation was prepared for informational purposes and is not intended to grant rights or impose obligations. Every reasonable effort has been made to assure the accuracy of the information within these pages.

- This publication is a general summary that explains certain aspects of the Clinical Laboratory Improvement Amendments (CLIA) Program, but is not a legal document. The official CLIA Program provisions are contained in the relevant laws, regulations, and rulings. Links to the source documents have been provided within the document for your reference.

- The Centers for Medicare & Medicaid Services (CMS) employees, agents, and staff make no representation, warranty, or guarantee that this compilation of CLIA information is error-free and will bear no responsibility or liability for the results or consequences of the use of this guide.

CMS DCLIQ ORGANIZATION



How many labs are there?

Approximate Number—Laboratories	314,895
Exempt States (New York and Washington)	15,317
Total Non-Exempt	299,578
CoC	17,603
CoW	255,549
CoA	16,082
PPM	25,661

Source: CMS database—October 2024

CMS CLIA goals for 2023

- Improved processes
  - Use of data to identify outliers in terms of survey findings, time spent on survey, team size
  - Adherence to enforcement timelines
  - Enhanced state oversight activities
- Modernizing CLIA
  - PT Rule implementation
  - Electronic Certificates
- Assessing the use of enforcement discretion and flexibilities during the PHE:
  - Remote review of pathology slides/data
  - Expedited review of CLIA applications
  - Contiguous site flexibilities
  - University non-CLIA COVID testing
  - COW testing authorization as soon as CLIA application is filed
  - COVID test result reporting
- Continuing our stakeholder engagement efforts

CMS CENTERS FOR MEDICARE & MEDICAID SERVICES

CLIA

Enforcement Timelines

March 1, 2022, through February 28, 2023:

Cases	97
Average pre-enforcement days	50.07
Average proposed days	120.73
Average imposed days	128.03
Average total enforcement days	138.49

Enforcement Timelines

March 1, 2022, through September 30, 2024:

Cases	30
Average pre-enforcement days	24.89
Average proposed days	22.1
Average imposed days	57.58
Average total enforcement days	66.29

Enforcement timeline improvements

Measure	Pre-reorganization	Since Reorganization	Percentage improvement
Average Pre-enforcement days	50.07	24.89	50.29%
Average Proposed Days	120.73	22.1	81.69%
Average Imposed Days	128.03	57.58	55.03%
Average Total Enforcement Days	138.49	66.26	52.15%

CMS CLIA goals for 2024

Year One Goals	Year Three Goals	Year Five Goals
• 50% of CLIA certificates will be electronic and available on-line • Issue Interpretive Guidance on the new Fee, histocompatibility, Personnel and Alternative Sanction rule. • Initiate action plan to address data that demonstrates survey inconsistencies related to team size, time spent on survey, citation rates. • Track enforcement actions to ensure consistency • Make CLIA Certificate of Compliance survey findings available of QCOR	• Implement Lab Director University • Revise enforcement letters for plain language and readability • Assess state budget allocations for consistency and fairness	• Develop other educational resources such as Technical Supervisor University, Technical Consultant University, etc. • Develop standardized survey process that is objective, consistent and computer assisted.

Additional Accomplishments

- Evaluated all proficiency testing providers to ensure compliance with the new PT regulations and are ready for implementation on 1/1/25
- We are currently 35% electronic and have developed a plan to convert to a fully electronic process in 2025
- Published guidance to address concerns with the BD Bactec blood culture vial shortage
- Approved additional certification for cytotechnologists based on stakeholder feedback
- Eliminated survey backlogs in 8 states
- Created the State Agency Monitoring database to track and assess communication with state agencies
- Re-engaged our regular communication with Accrediting Organizations and Exempt States

New Policy Memos

One policy memo since the last meeting:

- REVISIONS TO QSO-22-21-CLIA ORIGINALLY RELEASED ON JULY 11, 2022

This revision updates the table found on page 4 of this memo to correctly list two analytes, Cancer antigen (CA) 125 and Carcinoembryonic antigen (CEA), under Endocrinology (§§ 493.933).

This revision also corrects the reported units for CEA from “ng/dL” to “ng/mL”. The units were previously revised in the Federal Register, and this memo reflects the revision on page 9.

New Administrative Memos

Five Administrative memos were released since the last meeting:

- State Agency Performance Review (SAPR)—Fiscal Year 2024 (FY 2024)
- Fiscal Year (FY) 2025 Clinical Laboratory Improvement Amendments (CLIA) Budget Call Letter
- American Society for Clinical Pathology (ASCP) Board of Certification (BOC) Specialist in Cytology (SCT) as an Approved Board Certification for the Clinical Laboratory Improvement Amendments (CLIA) for Individuals Performing Testing in the Subspecialty of Cytology
- 2025 Clinical Laboratory Improvement Amendments (CLIA) Budget Call Letter
- Revisions to the Review and Approval of Plans of Correction (POCs) and CLIA Allegations of Compliance (AOCs)

Additional questions?

Thank you!

Gregg Brandush
Gregg.Brandush@CMS.HHS.GOV
312-353-1567

Policy memos can be found here:
https://www.cms.gov/medicare/health-safety-standards/quality-safety-oversight-general-information/policy-memos-states-and-cms-locations

Administrative memos can be found here:
https://www.cms.gov/medicare/health-safety-standards/quality-safety-oversight-general-information/administrative-information-memos-states-and-regions

FDA Update

CLIAC

November 6, 2024

Courtney H. Lias, Ph.D.
Office Director
Office of In Vitro Diagnostics (OIVD/OHT7)
Office of Product Evaluation and Quality (OPEQ)
CDRH | Food and Drug Administration

OHT7 Key Activities

Premarket Activities

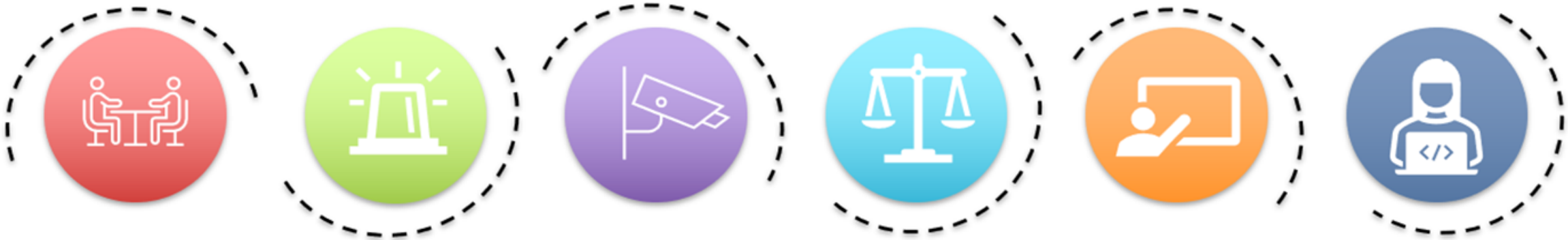
- PMA, 510(k), De novo request reviews
- Investigational Device Exemptions
- Humanitarian Device Exemptions
- Pre-submissions
- Breakthrough designation requests
- Premarket inspections
- CLIA waiver applications
- CLIA categorizations

Postmarket Activities

- Monitoring and Surveillance
- Postmarket Inspections
- Postmarket Studies
- Recalls
- Compliance and Enforcement Actions
- Safety communications

External Engagement & Outreach

- External training and engagement
- Public meetings
- Conferences
- Town Halls
- Inquiry responses



Emergency Use

- Emergency Use Authorizations
- Cross-agency collaborations
- Stakeholder engagement, including Town Halls

Guidance

- Issue new guidances
- Update existing guidances
- Training and webinars

Program Development & Operations

- Internal training
- Performance tracking
- Data reporting

Home Use/Home Access Tests

- Instrumental to enabling transition of care from the hospital to home
- Give patients health information from the privacy of home
- Some may detect possible health conditions when patients have no symptoms, enabling early treatment
- Some may monitor conditions to allow frequent changes in treatment

ALLTEST FENTANYL URINE TEST CASETTE

OTC at-home test for the preliminary detection of fentanyl in urine

ACON FLOWFLEX COVID-19 TEST

OTC home use visually-read antigen test for COVID-19

Home Use/Home Access Tests

Considerations for Home Use Testing

- Type of specimen
- Method of specimen collection
- Complexity of testing (e.g., pre-analytical incubations)
- Toxicity of reagents
- Risks of misinterpretation, non-specific results
- Need for HCP input

Home Use/Home Access Tests

- FDA has long encouraged development of at-home tests - >400 OTC tests authorized in the last 10 years alone.
- OTC tests like pregnancy tests and blood glucose tests benefit millions of Americans each year.
- FDA continues working closely with developers of OTC tests – and has authorized many types of OTC tests, including these examples:

- OTC COVID-19 tests
- OTC blood glucose meters
- OTC pregnancy tests
- OTC drugs of abuse tests
- OTC PT-INR tests to monitor safety in patients on warfarin
- OTC cholesterol tests
- OTC HbA1c tests to monitor blood glucose control in people with diabetes
- OTC genetic risk tests

CDRH Initiates the Reclassification Process for Most High Risk IVDs

- Proposed reclassification for most IVDs that are currently class III (high risk) into class II (moderate risk)
  - Primarily infectious disease and companion diagnostic IVDs
- **September 25, 2024**: FDA proposed reclassification of antigen, antibody, and nucleic acid-based Hepatitis B Virus assay devices **(comment period ends 11/25/2024)**
- **October 23, 2024:** FDA issued a final order to reclassify cytomegalovirus (CMV) deoxyribonucleic acid (DNA) quantitative assay devices intended for transplant patient management
- Reclassifications may lead to increased access

Federal Register: Proposed Rule
Federal Register: Final Rule

Highly Pathogenic Avian Influenza (HPAI) A(H5N1)

- Current assessment of test detection capability
  - Conducting updated reactivity risk assessments for flu IVDs
  - The results of these analyses are important to ensure that tests are available which are expected to detect H5N1
- Working closely with Federal Partners to monitor the situation
- Update to the Influenza Diagnostic Tests web page

PHE Tests Authorized as of October 29, 2024

290

COVID Molecular diagnostic tests

Including:

- 24 Multi-analyte (i.e., SARS-CoV-2 + Influenza)
- 20 Point-of-care
- 72 Home collection
  - 16 Direct-to-consumer
  - 5 Multi-analyte
  - 14 Saliva home collection
- 4 Over-the-counter (OTC) at-home tests

78

COVID-19 Serology and other immune response tests

77

COVID-19 Antigen diagnostic tests

Including:

- 72 Point-of-care
- 38 Over-the-counter (OTC) at-home tests
- 19 Multi-Analyte

8

mpox NAAT diagnostic tests

Including:

- Automated
- Point-of-care
- Tests developed in collaboration with ITAP

Do Not Use Cue Health's COVID-19 Tests Due to Risk of False Results

May 13, 2024: FDA issued a safety communication warning home test users, caregivers, and health care providers not to use Cue Health's COVID-19 Tests due to increased risk of false results

October 9, 2024: FDA revoked the Emergency Use Authorizations for both of Cue Health's COVID-19 test kits, the Cue COVID-19 Test, previously authorized for point-of-care use, and the Cue COVID-19 Test for Home and Over The Counter (OTC) Use, previously authorized for home use

October 15, 2024: FDA classified Cue Health's voluntary recall of their two COVID-19 tests as a class II recall

Safety Communication

ITAP for RNA Point-of Care (POC) Diagnostics: "Test to Treat"

U.S. FOOD & DRUG ADMINISTRATION

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FDA NEWS RELEASE

FDA Permits Marketing of First Point-of-Care Hepatitis C RNA Test

Test Enables Single-Visit Testing and Treatment for Hepatitis C

Share | Post | Linkedin | Email | Print

More Press Announcements

mediate Release: June 27, 2024

Español

Content current as of: 06/27/2024

Regulated Product(s) Medical Devices

Today, the U.S. Food and Drug Administration granted marketing authorization to Cepheid for the Xpert HCV test and GeneXpert Xpress System, the first hepatitis C virus (HCV) test that can be used to bring diagnosis to appropriately certified point-of-care settings for individuals at risk for hepatitis C. The test may be performed in

Cepheid Xpert HCV test and GeneXpert Xpress System: Granted June 27, 2024

Independent Test Assessment Program (ITAP) | National Institute of Biomedical Imaging and Bioengineering (nih.gov)

ITAP for HCV POC Diagnostics - POCTRN - GAITS

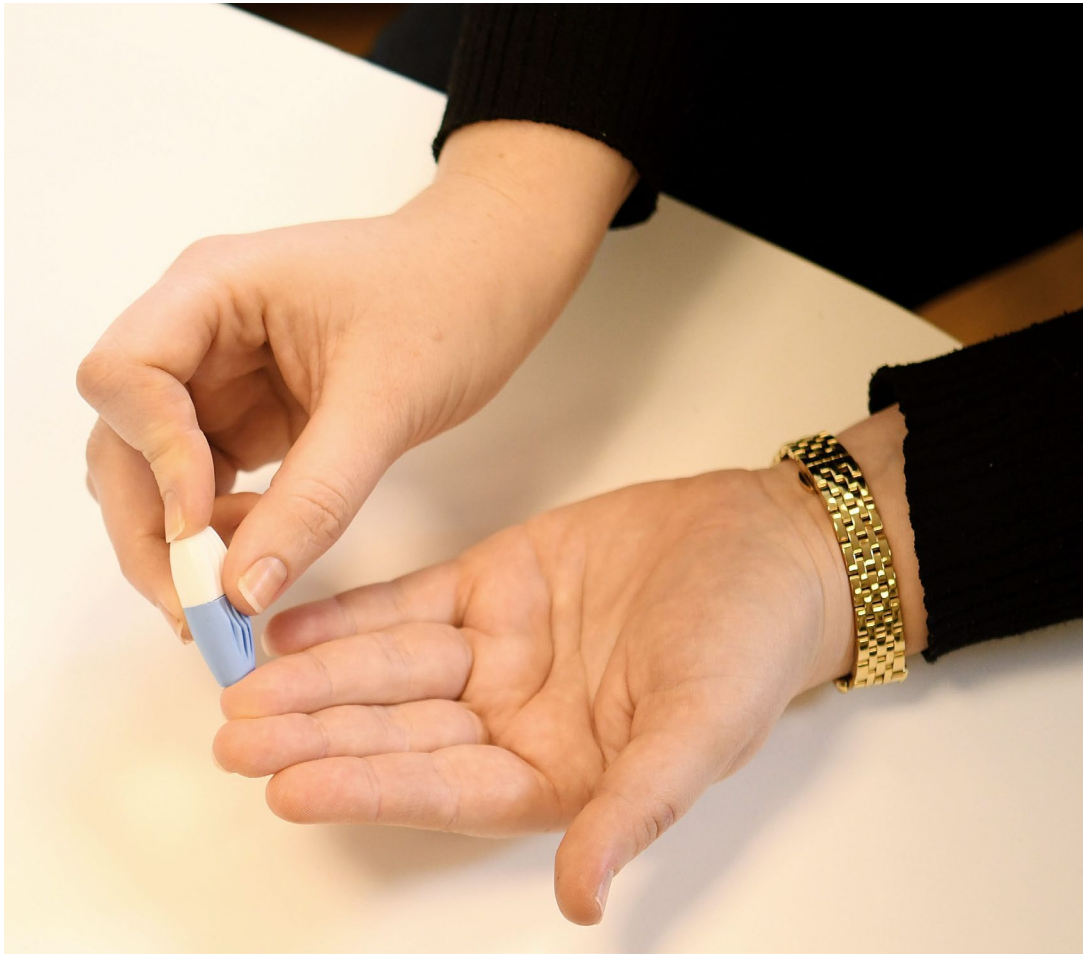
Press Release

FDA Marketing Authorization Enables Increased Access to First Step of Syphilis Diagnosis

NOWDiagnostics First To Know Syphilis Test: Granted August 16, 2024

- First at-home, over-the-counter test to detect Treponema pallidum (syphilis) antibodies in capillary whole blood
- The test provides an at-home result without a prescription, in approximately 15 minutes, which individuals can use to better inform next steps with a health care provider

Press Release



FDA Clears First Device to Enable Automated Insulin Dosing for Individuals with Type 2 Diabetes

Insulet SmartAdjust Technology:
Cleared August 26, 2024

- First automated insulin delivery (AID) system indicated for both type 1 and type 2 diabetes
- Automated insulin dosing technology previously available only for people with type 1 diabetes. This clearance helps expand access to this important diabetes management tool to millions of adults living in the U.S. with type 2 diabetes

Press Release

FDA Authorizes Marketing of First Home Flu and COVID-19 Combination Test Outside of Emergency Use Authorities

Healgen Rapid Check COVID-19/Flu A&B Antigen Test: Granted October 7, 2024

- Intended for the qualitative detection and differentiation of influenza A, and influenza B nucleoprotein antigens and SARS-CoV-2 nucleocapsid antigen directly in anterior nasal swab samples

- First over-the-counter (OTC) test that can detect influenza to be granted marketing authorization using a traditional premarket review pathway

Press Release

Colorectal Cancer Screening Tests

Geneoscopy ColoSense: Approved May 3, 2024

- An RNA-FIT test for the qualitative detection of colorectal neoplasia associated RNA markers and for the presence of occult hemoglobin in human stool

Guardant Health Shield: Approved July 26, 2024

- A qualitative in vitro diagnostic test intended to detect colorectal cancer derived alterations in cell-free DNA from blood collected in the Guardant Blood Collection Kit

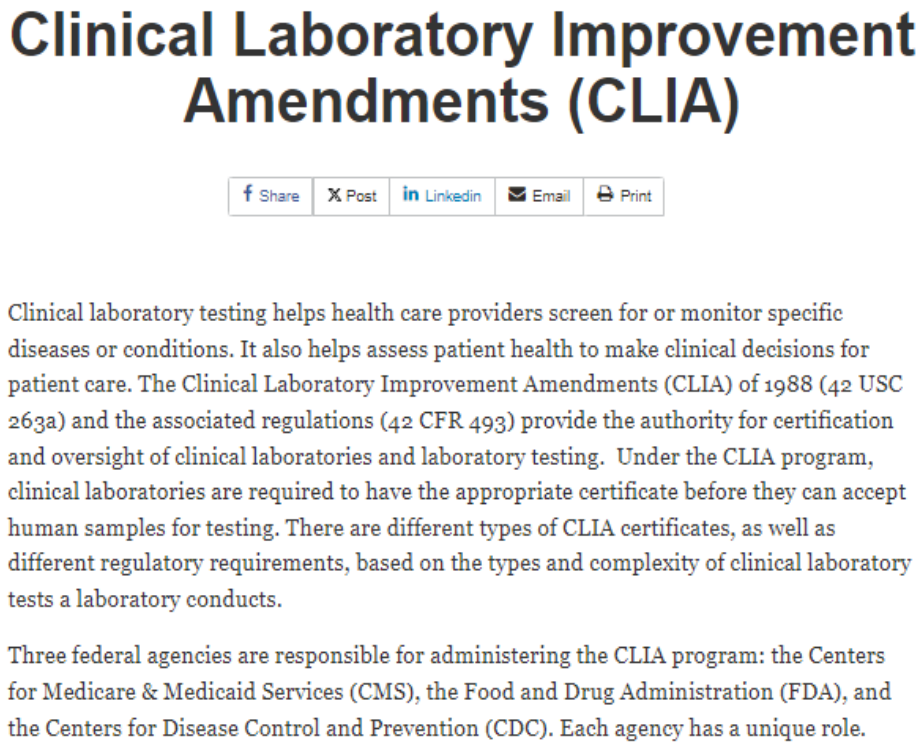
Exact Sciences Cologuard Plus: Approved October 3, 2024

- A qualitative in vitro diagnostic test intended for the detection of colorectal neoplasia-associated DNA markers and for the presence of occult hemoglobin in human stool, performed on samples collected using the Cologuard Plus Collection Kit

Summary

Ways to interact with us:

- FDA CLIA Webpage
- Office of In Vitro Diagnostics Webpage
- Medical Device Safety Communications
- Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program
- For CLIA-related questions: CLIA@fda.hhs.gov
- For COVID-19 Diagnostics questions: Covid19DX@fda.hhs.gov
- For mpox Diagnostics questions: MPXdx@fda.hhs.gov



U.S. FOOD & DRUG ADMINISTRATION

Thank You

CLIAC Biosafety Workgroup Final Report

CLIAC November 6-7, 2024

Michael Pentella, PhD, D(ABMM), Workgroup Chair

Clinical Laboratory Improvement Advisory Committee (CLIAC) Recommendations

CLIAC has issued five recommendations that address safety:

February 2001	April 2015	April 2016	November 2016	November 2019
Wild poliovirus containment	Emerging infections	Biosafety in clinical laboratories: an unmet national need	Laboratory-associated incident reporting system	Laboratory workforce: safety included

https://www.cdc.gov/cliac/php/meetings/?CDC_AAref_Val=https://www.cdc.gov/cliac/past-meetings.html

CLIA Regulations - Safety

Definitions

Operator means the individual or group of individuals who oversee all facets of the operation of a laboratory and who bear primary responsibility for the safety … The term includes –

(1) A director of the laboratory…; and

(2) The members of the board of directors and the officers of a laboratory…

§ 493.1101 Standard: Facilities.

(d)Safety procedures must be established, accessible, and observed to ensure protection from physical, chemical, biochemical, and electrical hazards, and biohazardous materials.

Subpart R - Enforcement Procedures § 493.1804 General considerations.

(a) *Purpose.* The enforcement mechanisms set forth in this subpart have the following purposes:

(1) To protect all individuals served by laboratories against substandard testing of specimens.

(2) To safeguard the general public against health and safety hazards that might result from laboratory activities.

CLIAC Biosafety Workgroup

Workgroup Charge

- Charged with providing input to CLIAC for consideration in making recommendations to the Department of Health and Human Services (HHS) on the potential additions to the CLIA regulations and the need for solutions that will provide a safe working environment for the nation's clinical and public health laboratories.

Workgroup Members

- Michael A. Pentella, PhD, D(ABMM) - Chair
- Víctor R. De Jesús, PhD - Designated Federal Officer
- Nancy Cornish, MD - Workgroup CDC Ex Officio
- Lane N. Vause, MS, MPH, MLS(ASCP)^{MBCM}, CPH - Workgroup CMS Ex Officio
- Amy Zale, MT(ASCP) - Workgroup FDA Ex Officio
- Latess Atkins-Banks, MBA, MLS(ASCP)^{CM}
- Kathleen G. Beavis, MD
- Andrew Bryan, MD, PhD, D(ABMM)
- Sheldon Campbell, MD, PhD
- Jamie P. Deeter, MS, PhD
- Marian Downing, RBP, CBSP, SM(NRCM)
- Heather Duncan, MPH, MT(ASCP), CQA(ASQ)
- Shoolah H. Escott, MS, MT(ASCP)
- Shawn G. Gibbs, PhD, MBA, CIH
- Dan Hammersley, ASP
- Andy Hay
- David Hill, MEM, CIH
- Marianne Kim, PhD
- Cristine C. Lawson, PhD, RBP, CBSP
- Tracie Nichols, MS, MLS (ASCP), SBB^{CM}, CABP, CQA (ASQ)
- Luis Ochoa Carrera, MS, IFB^{CP}
- Elizabeth Palavecino, MD, FACP
- Marcia Pindling, DMH, MS, RBP (ABSA), MT, M(ASCP)
- James Pusavat, BSMT, MLS(ASCP), CLS(NCA), SM(ASCP)
- Kimberly Starr, PhD, D(ABMM)
- April Veoukas, JD

Question 1

- In vitro diagnostic product (IVD) instrument design plays a key role in mitigating biosafety. How can biosafety issues for instruments in use and new instruments in the design phase be addressed?
  - 1a - How do manufacturers currently assess biosafety considerations for established instruments and instruments being developed?
    - Are there user communities in which biosafety issues are discussed? If so, what are they? Are manufacturers included in these communities?
    - Are there mechanisms that facilitate collaboration between manufacturers and clinical laboratories to incorporate or improve biosafety features?

Question 1b and c

- 1b - In designing new instruments, what biosafety considerations are there?
  - Decontamination/sterilization?
  - Use of disposable parts?
  - Others?
- 1c - Is there collaboration between manufacturers and clinical laboratorians during the design stage for new instrumentation to improve biosafety features?

Q1: Workgroup Discussion & Consensus

- Laboratories should have a requirement to perform a risk assessment on all instrumentation currently in use and before purchasing new equipment.
- Laboratory equipment manufacturers have protocols for disinfection and/or decontamination, but they are mainly from the standpoint of the instrument to avoid or prevent cross-contamination for the specific agent they are detecting.
    - Often, instructions are unclear, hard to locate and focused on the patient versus the operator.
- Robust model systems and appropriate assays should be created to generate biologically meaningful decontamination data that can be extrapolated to an emerging pathogen situation.
- Instrument cleaning and decontamination guidance should be standardized and easily identified in the instruction manual provided to the end user.
    - A centralized location, repository, or website that manufacturers can use to post such guidance would be useful.

Question 2

- 2 - Laboratories handle specimens that contain unknown pathogens routinely. What assurance is there that proper biosafety activities are established, effectively provided/communicated, and followed?
  - 2a - Are training materials for laboratorians available that focus on instrument operation, and cleaning and disinfection practices?
    - Do currently available biosafety training materials include sufficient information regarding instrument disinfection? What should be included in these trainings?
  - 2b - Are there mechanisms that would ensure annual biosafety training and/or competency assessment of laboratory staff?

Q2: Workgroup Discussion & Consensus

- There is inadequate biosafety training related to instrument operation and decontamination.
  - Training should be developed to include service engineers, application specialists, trainers, and others who are not necessarily medical technology trained.
  - The laboratory director is responsible for ensuring that individuals entering the laboratory are trained in disinfection and decontamination cleaning procedures, especially maintenance procedures.
- Partnerships with manufacturers are essential in developing training for new instrumentation.
- Training should be provided for the entire laboratory process with people from different perspectives, i.e., surgical pathology, core facility, and hematology.
  - Ideally, the training will include case studies and provide the learner with an understanding of the source of the dangers, how to identify those hazards, and how to start mitigation.
- No standardized mechanisms are in place to assess biosafety competency adequately, development is needed.

Question 3

Currently, the Facilities standard at § 493.1101(d) indicates that "Safety procedures must be established, accessible, and observed to ensure protection from physical, chemical, biochemical, and electrical hazards, and biohazardous materials."

- 3 - What additions to the CLIA regulations could be made to ensure that laboratories are required to have policies and procedures addressing laboratory biosafety?
- 3a - Should the CLIA regulations be updated to include additional safety standards as related to facilities that could include, but not be limited to, the items listed below?
  - Proper workspace ventilation.
  - Proper decontamination processes.
  - Appropriate biosafety equipment and personal protective equipment available.
  - Requirement to report results of highly infectious organisms, potential agents of bioterrorism, and unusual multi-drug resistant organisms to State Public Health laboratories or CDC as required by Federal, State, or local government authority.

Question 3b

Currently, the General Considerations Standard at § 493.1804(a)(2) indicates that “To safeguard the general public against health and safety hazards that might result from laboratory activities.”

- 3b - Should the CLIA regulations be updated to include additional safety standards related to General considerations?

Q3: Workgroup Discussion & Consensus

- Revising CLIA guidelines might have cost implications and should be based on the lab specific risk assessment.
- FDA review does not include biosafety aspects but is more in the context of the potential for false positive or negative results.
- Manufacturers should refine and provide the scope of decontamination of laboratory equipment through the risk assessment process and provide this information to end users.
- Defining the range of risk assessment was emphasized. It was agreed that the language should be comprehensive, including hazard assessment, mitigation, and performance monitoring.
- Reporting requirements for the identification of certain pathogens should be kept general but noted that better synthesis and coordination are needed from the agencies on reporting requirements.

Question 4

- Clear instructions and communication are key to addressing biosafety. Therefore,
  - 4a - How can manufacturers and clinical laboratories work together to provide clear, readily available biosafety instructions for each phase of testing, cleaning and disinfection practices, and maintenance of the instrument?
  - 4b - What resources are available for manufacturers to gain biosafety-related input to develop appropriate instructions (e.g., Environmental Protection Agency lists, Occupational Safety and Health Administration regulations)?
  - 4c - How can manufacturers gain input from biosafety professionals to aid the development of supplemental biosafety testing instructions for end users and service representatives?
  - 4d - How can non-regulatory organizations (e.g., the Clinical and Laboratory Standards Institute, the International Organization for Standardization), professional societies (e.g., The Association for Biosafety and Biosecurity, The American Society for Microbiology), and other interested parties assist in facilitating the process for manufacturers and laboratories?

Q4: Workgroup Discussion & Consensus

- Increased collaboration between equipment manufacturers and clinical and public health laboratories was encouraged.
    - It was suggested that an organizational approach between the interested parties would be more appropriate for developing these resources.
- The workgroup suggested that the FDA should explore adding a requirement that the manufacturer provide biosafety guidance as part of product review and clearance.
- A common theme was the notion that a space should be created to serve as a centralized repository for biosafety information that both the manufacturers and end-users can access.
- The workgroup discussed updating CLIA requirements to include biosafety training as part of testing personnel competency requirements. It requested the development of an implementation guide.
- It was clarified and reinforced that the manufacturer's instructions for use must be sufficient for users and manufacturers' service personnel to accomplish disinfection and provide sufficient detail to allow incorporation into the laboratory's site-specific risk assessment.

Workgroup Agreements

1. The workgroup agreed that a standardized definition of a biosafety risk assessment should be developed and added to 42 CFR 493.2.
2. The workgroup agreed that language in the definition of a biosafety risk assessment should be comprehensive about the risk assessment, including hazard assessment, mitigation, management, and performance monitoring.
3. The workgroup agreed that laboratories should be required to perform a risk assessment on all instrumentation currently in use. Before implementation, laboratories should consider biosafety risks when purchasing new equipment and must complete a risk assessment (analogous to analytic verification).
4. The workgroup agreed that 42 CFR 493.1804(a)(2) should be expanded to clarify that laboratory workers and, in turn, the general population should be safeguarded.
5. The workgroup agreed that a Food and Drug Administration (FDA) requirement(s) on biosafety risk assessment for device approval would support clinical laboratory biosafety and the health of the public.

Workgroup Agreements

6. The workgroup agreed that it is the laboratory's responsibility to obtain the written equipment disinfection instructions and practices, preferably before purchase. Additionally, end users should incorporate the manufacturer’s detailed instructions and practices into their biosafety risk assessments and routine practices.
7. The workgroup agreed that CLIA requirements should be revised to include biosafety training as part of testing personnel competency requirements.
8. The workgroup agreed that there is a need for annual biosafety competency assessments.
9. The workgroup agreed that there is value in increased collaboration between equipment manufacturers, clinical and public health laboratories, and regulatory agencies to improve knowledge of instrument risks and hazards and effective mitigation and decontamination practices. Additional research is needed to determine the best path forward.

THE CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC)
2024 BIOSAFETY WORKGROUP

MEETING SUMMARY REPORT

Workgroup Charge

The CLIAC Biosafety Workgroup is charged with providing input to CLIAC for consideration in making recommendations to the Department of Health and Human Services (HHS) on the potential additions to the CLIA regulations and the need for solutions that will improve the safety of laboratory professionals, their colleagues, and the environment.

Workgroup Agreements

1. The workgroup agreed that a standardized definition of a biosafety risk assessment should be developed and added to 42 CFR 493.2.
2. The workgroup agreed that language in the definition of a biosafety risk assessment should be comprehensive about the risk assessment, including hazard assessment, mitigation, management, and performance monitoring.
3. The workgroup agreed that laboratories should be required to perform a risk assessment on all instrumentation currently in use. Before implementation, laboratories should consider biosafety risks when purchasing new equipment and must complete a risk assessment (analogous to analytic verification).
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5. The workgroup agreed that a Food and Drug Administration (FDA) requirement(s) on biosafety risk assessment for device approval would support clinical laboratory biosafety and the health of the public.
6. The workgroup agreed that it is the laboratory's responsibility to obtain the written equipment disinfection instructions and practices, preferably before purchase. Additionally, end users should incorporate the manufacturer’s detailed instructions and practices into their biosafety risk assessments and routine practices.
7. The workgroup agreed that CLIA requirements should be revised to include biosafety training as part of testing personnel competency requirements.
8. The workgroup agreed that there is a need for annual biosafety competency assessments.
9. The workgroup agreed that there is value in increased collaboration between equipment manufacturers, clinical and public health laboratories, and regulatory agencies to improve knowledge of instrument risks and hazards and effective mitigation and decontamination practices. Additional research is needed to determine the best path forward.

Workgroup Meeting #1 Summary - February 12, 2024

In vitro diagnostic product (IVD) instrument design plays a key role in mitigating biosafety issues that arise during routine use and maintenance schedules. How can interested parties better address biosafety for already established IVD instruments and IVD instruments currently under development?

a. What mechanisms/best practices do manufacturers currently use to assess biosafety considerations for established IVD instruments and IVD instruments currently under development?
   i. Are there current mechanisms where end users can discuss/highlight biosafety issues with established IVD instruments within the end-user community and/or with the manufacturer? If so, what are they? How can manufacturers be included if they are currently not included?
   ii. Are there mechanisms currently in place or that can be developed that would facilitate collaboration between manufacturers and a variety of clinical laboratory representatives during the use and maintenance of existing IVD instrumentation to incorporate or improve biosafety features?

b. When developing new IVD instrumentation, what considerations are typically given to biosafety with respect to instrument design (e.g., the robustness of instrument parts/materials to routine decontamination/sterilization procedures, use of disposable parts in areas of the instrumentation that are more at risk of contamination)?

c. c. Are there mechanisms currently in place or that can be developed to facilitate collaboration between manufacturers and a variety of clinical laboratory representatives during the design stage for new IVD instrumentation under development to incorporate or improve biosafety features?

Workgroup Discussion and Comments

- A consensus was reached that laboratories should have a requirement to perform a risk assessment on all instrumentation currently in use and also before purchasing new equipment.
  - There is not currently a framework to conduct a risk assessment, but an ideal framework would address safety across the entire pre-analytic, analytic, and post-analytic aspects of the test system.
  - The risk assessment will need to include instructions for using the equipment under normal conditions and during extended periods of time, such as surge testing periods, and should include guidance for decontamination and disinfection.
  - Guidelines and training on how to conduct a biological risk assessment should be developed.
- Laboratory equipment manufacturers do have protocols for disinfection and/or decontamination, but they are mainly from the standpoint of the instrument itself to avoid or prevent cross-contamination for the specific agent they are detecting.
- It was emphasized that often, these instructions are unclear and hard to locate and are focused on the patient versus the operator.
  - Decontamination guidance should be provided for an instrument and must address the actual design, aerosol prevention, cross-contamination, and exposure to risks and hazards.
    - This should be viewed as a shared responsibility, one on the design side and one on the assessment side.
    - The conversations with the manufacturer should be in the early phase about what type of materials they can use that would withstand several different types of decontamination materials or how it would undergo sterilization.

        - Robust model systems and appropriate assays should be created to generate biologically meaningful decontamination data that can be extrapolated to an emerging pathogen situation.
        - Instrument cleaning and decontamination guidance should be standardized and easily identified in the instruction manual provided to the end user.
        - A centralized location, repository, or website that manufacturers can use to post such guidance would be useful.
    - It was agreed that the responsibility for the risk assessment is shared between the manufacturer and the laboratory, but it was noted that the laboratory needs information from the manufacturer to identify the critical parts of the instrument and specifically what to use for decontamination.

Laboratories receive and handle specimens that contain unknown pathogens routinely. How can interested parties ensure proper biosafety activities for end users are established, effectively provided/communicated, and followed?

a. Are there widely available training materials for laboratory professionals that focus on instrument operation and cleaning and disinfection practices?
    i. Do currently available biosafety training materials include sufficient information regarding instrument disinfection? If not, what minimum information should be included in these trainings?
b. Are there mechanisms in place or that can be developed by laboratories that would ensure annual biosafety training and/or competency assessment of laboratory staff?

Workgroup Discussion and Comments

- A consensus was reached that there is inadequate biosafety training related to instrument operation and decontamination.
    - Training should be developed to include service engineers, application specialists, trainers, and others who are not necessarily medical technology trained.
    - The laboratory director is responsible for ensuring that individuals entering the laboratory are trained in disinfection and decontamination cleaning procedures, especially maintenance procedures.
- Partnerships with manufacturers are essential in developing training for new instrumentation.
- Training should be provided for the entire laboratory process with people from different perspectives, i.e., surgical pathology, core facility, and hematology.
    - Ideally, the training will include case studies and provide the learner with a more basic understanding of where the dangers are coming from, how to identify those hazards, and how to start mitigation.
- It was acknowledged that no standardized mechanisms are in place to assess biosafety competency adequately, and they should be developed.

Workgroup Meeting #2 Summary - June 28, 2024

What additions to the CLIA regulations could be made to ensure that laboratories are required to have policies and procedures addressing laboratory biosafety?

a. Currently, the Facilities standard at §493.1101(d) indicates that "Safety procedures must be established, accessible, and observed to ensure protection from physical, chemical, biochemical, and electrical hazards, and biohazardous materials." Should the CLIA regulations be updated to

include additional safety standards as related to facilities that could include, but not be limited to, the items listed below?

i. Proper workspace ventilation to safely handle contaminated specimens or pathogenic organisms at the appropriate biosafety level.
ii. Proper decontamination processes in place to help minimize contamination for the environment and instrumentation.
iii. Appropriate biosafety equipment and personal protective equipment are available in accordance with the appropriate biosafety level.
iv. Requirement to report results of highly infectious organisms, potential agents of bioterrorism, and unusual multi-drug resistant organisms to State Public Health laboratories or CDC as required by Federal, State, or local government authority.

b. Currently, the General Considerations Standard at §493.1804(a)(2) indicates that "To safeguard the general public against health and safety hazards that might result from laboratory activities." Should the CLIA regulations be updated to include additional safety standards related to General considerations?

Workgroup Discussion and Comments

- The workgroup discussed updating the CLIA regulations to include additional safety standards related to the facility.
- The workgroup acknowledged that revising CLIA guidelines might have cost implications for the laboratory and should be based on the risk assessment process to address the site-specific needs of each laboratory category.
- It was noted that a standardized definition of a 'risk assessment' is currently lacking and should be developed and added to 42 CFR 493.2.
- The workgroup reviewed 42 CFR 493.1101 and recommended clarifying that the risk assessment process should guide the establishment of safety procedures.
- An agreement among all that in an ideal scenario, a risk assessment should be performed in the laboratory and emphasized that the manufacturer, as part of the development process, should perform a risk assessment in anticipation of the end-user application in a typical hospital/clinical laboratory.
- The workgroup discussed the potential for incorporating a risk assessment requirement into the CLIA regulations at 42 CFR 493.1253 [Standard: Establishment and verification of performance specifications].
- It was agreed that the manufacturer should refine and provide the scope of decontamination of laboratory equipment through the risk assessment process and provide this information to the end user.
- The FDA agrees that it is a manufacturer's issue to provide decontamination instructions to the end user and is working with the CDC on ways the manufacturer can advise the end user on adequate decontamination procedures, including what chemicals can be used and a clear definition of responsibility.
- The workgroup agreed that PPE should be identified during the risk mitigation component of the risk assessment process, and training should be provided to staff on the correct use of PPE, and this correct use of safety PPE should be part of the competency assessment.
- An agreement was reached that reporting requirements for the identification of certain pathogens should be kept general but noted that better synthesis and coordination are needed from the agencies on reporting requirements.
- The workgroup agreed that 42 CFR 493.1804(a)(2) should be expanded to clarify that the laboratory worker should be safeguarded as well as the general population.

Clear instructions and communication are key to addressing biosafety. Therefore,

a. How can manufacturers and clinical laboratories work together to provide clear, readily available biosafety instructions for each phase of testing, cleaning and disinfection practices, and maintenance of the instrument?
b. What resources are available for manufacturers to gain biosafety-related input to develop appropriate instructions (e.g., Environmental Protection Agency lists, Occupational Safety and Health Administration regulations)?
c. How can manufacturers gain input from biosafety professionals to aid in the development of supplemental biosafety testing instructions for end users and service representatives?
d. How can non-regulatory organizations (e.g., the Clinical and Laboratory Standards Institute, the International Organization for Standardization), professional societies (e.g., The American Biological Safety Association, The American Society for Microbiology), and other interested parties assist in facilitating the process for manufacturers and laboratories?

Workgroup Discussion and Comments

- The workgroup agreed that manufacturers should work with the end-user during the design stage and before regulatory approval to address possible biosafety implications. However, it was noted that the end user is not currently involved in the design phase.
- The workgroup suggested that the FDA should explore adding a requirement that the manufacturer provide biosafety guidance as part of product review and clearance.
- A common theme was the notion that a space should be created to serve as a centralized repository for biosafety information that both the manufacturers and end-users can access.
- The workgroup discussed updating CLIA requirements to include biosafety training as part of testing personnel competency requirements. It requested the development of an implementation guide.
- The workgroup emphasized the importance of hiring competent biosafety professionals with laboratory experience to work with manufacturers during the design process but noted it was beyond the scope of the workgroup.
- It was suggested that an organizational approach between the interested parties would be more appropriate for developing these resources.

Workgroup Meeting #3 Summary - August 23, 2024

Workgroup Discussion and Comments

- The workgroup discussed updating the CLIA regulations to include additional safety standards related to the facility.
- It was agreed that risk assessments are needed.
  - The group discussed linking the risk assessment into the test verification and validation process, although it might be redundant.
  - Risk assessment should occur on each test system, including those without instrumentation, for each testing stage.
- Risk assessment vs risk management was discussed, and it was noted that there is a lack of comprehensive understanding.
- Defining the range of risk assessment was emphasized. It was agreed that language should be comprehensive about the risk assessment, including hazard assessment, mitigation, and performance monitoring.
  - The need for resources and references was discussed, and it was agreed that these should be included in the summary report to provide background.

        - These will be included in the summary report as an Appendix.
        - All workgroup members were encouraged to provide resources that would benefit the group and give context to CLIAC.
- The workgroup again agreed that 42 CFR 493.1804(a)(2) should be expanded to clarify that laboratory workers and the general population should be safeguarded.
- It was reaffirmed that the FDA review does not include biosafety aspects but is more in the context of the potential for cross-contamination or cross-carriage of the samples themselves to determine if there's a potential for false positive or negative results.
- A consensus was reached that the equipment manufacturer's instructions must include disinfection practices.
- It was noted that test categorization, including if there's a public health emergency in the EUA process, is within the scope of the CLIA program and the CLIA regulations; however, medical device approval is within another regulatory statement law, the Federal Drug and Cosmetic Act.
- Increased collaboration between equipment manufacturers and clinical and public health laboratories was strongly encouraged.

Workgroup Meeting #4 Summary - September 13, 2024

Workgroup Discussion and Comments

- The summary from the previous meeting was reviewed, and items below were clarified:
    - It was clarified and reinforced that the manufacturer's instructions for use must be sufficient for users and manufacturers' service personnel to accomplish disinfection and provide sufficient detail to allow incorporation into the laboratory's site-specific risk assessment.
    - Collaboration between the manufacturers and equipment users was again stressed and recommended.
    - It was clarified that the assessment of biosafety competencies should be performed annually.
- The workgroup reviewed and refined the current list of workgroup agreements in preparation for the November 6-7, 2024, workgroup report and CLIAC discussion.

References Provided by Workgroup Members

Citation:

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- Herstein, J. J., S. A. Buehler, A. B. Le, J. J. Lowe, P. C. Iwen and S. G. Gibbs (2019). "Clinical Laboratory Equipment Manufacturer Policies on Highly Hazardous Communicable Diseases." Public Health Rep **134**(4): 332-337.
- Le, A. B., C. E. Figi, J. J. Herstein, P. C. Iwen, S. A. Buehler, J. J. Lowe and S. G. Gibbs (2024). "Clinical laboratory equipment manufacturers' lack of guidance for high consequence pathogen response is a critical weakness." Infect Control Hosp Epidemiol: 1-3.

ISO: International Organization for Standardization

- ISO 9001:2015, Quality management systems — Requirements
- ISO 15189:2012, Medical laboratories — Requirements for quality and competence
- ISO 15190:2003, Medical laboratories — Requirements for safety
- ISO 45001:2018, Occupational health and safety management systems — Requirements with guidance for use
- ISO Guide 73:2009, Risk management — Vocabulary
- ISO 13485:2016, Medical devices – Quality management systems – Requirements for regulatory purposes
- ISO/IEC 17025:2017, General requirements for the competence of testing and calibration laboratories
- ISO 31000:2018, Risk Management – Guidelines

WHO: World Health Organization

- Laboratory biosafety manual, fourth edition. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition, and associated monographs).
- Decontamination and waste management. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition, and associated monographs).
- Risk assessment. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition, and associated monographs).

Other

- CEN Workshop Agreement 15793:2011, Laboratory biorisk management
- CEN Workshop Agreement 16393:2012, Laboratory biorisk management — Guidelines for the implementation of CWA 15793:2008
- APHL Laboratory Biosafety Competency Assessment Form https://www.aphl.org/programs/preparedness/Documents/APHL%20Approved%20Conversation-Based%20Biosafety%20Competency%20Assessment%20Form.pdf
- ABSA OSHA Alliance, Biological Safety Professional Competency Fact Sheet: https://absa.org/wp-content/uploads/2018/05/OSHABSOcompetencyFactSheet.pdf
- Sandia National Laboratories: *Core Biorisk Management Document Templates,* https://gcbs.sandia.gov/core-documents/
- The Canadian Biosafety Guideline – Local Risk Assessment: https://www.canada.ca/en/public-health/services/canadian-biosafetystandards-guidelines/guidance.html

Appendix A

CLIAC Biosafety Workgroup
Charge, Topics, and Discussion Questions
Workgroup Terms of Engagement

BACKGROUND

From a historical perspective, laboratory biosafety was initially designed to address the dangers of working with dangerous pathogens in research laboratories. For years, laboratory biosafety efforts were almost exclusively focused on research facilities. Recently, there's been a broader recognition that clinical laboratories may encounter dangerous pathogens, which can be present in patient specimens without the laboratory staff's knowledge. A laboratory accident or laboratory-acquired infection could affect the laboratory staff, others around them, and their environment, and fears about inadequate biosafety can paralyze a clinical laboratory and jeopardize patient care. The underlying weakness of clinical laboratory biosafety in the United States became clear when Ebola spread from West Africa to the United States in 2014. Soon after the first Ebola patient appeared in the United States, many of the largest commercial laboratory companies, all well-versed in handling specimens that contain dangerous pathogens, publicly announced they would not accept blood or tissue samples from suspect Ebola patients. Many laboratory instrument manufacturers followed suit. Some indicated that their warranties called for the incineration of their equipment after use with samples from suspect Ebola patients. Others explained that their technicians would not service equipment from isolation wards used for suspected Ebola patients. In 2014, CAP surveyed 28 health systems and more than 350 hospitals during the Ebola crisis. Only four of 17 respondents indicated they would allow suspected or confirmed Ebola virus disease specimens into their laboratories. Of those four, one would restrict testing to a BSL-3 laboratory and strongly discourage sending clinical specimens to the laboratory for testing. This almost complete shutdown of clinical laboratory testing in the US for suspected Ebola patients had significant consequences. Between July and November 2014, local health departments and healthcare providers acknowledged that complete blood counts, liver function tests, and serum chemistries were regularly deferred until a negative Ebola virus test result was obtained. Individuals who had recently traveled to or from Africa with fever and malaise symptoms were routinely refused malaria testing until Ebola had been ruled out. As a result, most malaria patients did not receive the proper and timely intravenous antiviral treatment. According to one Centers for Disease Control and Prevention (CDC) study, at least two persons who tested negative for Ebola died from other causes because of severely delayed diagnoses and treatment. The gaps discovered during the Ebola outbreak are documented in *Clinical Laboratory Biosafety Gaps: Lessons Learned from Past Outbreaks Reveal a Path to a Safer Future*, which discusses critical gaps in clinical laboratory biosafety, including issues related to the use and disinfection of laboratory instruments.

Over the last 20 years, infectious disease outbreaks, epidemics, and pandemics have occurred, putting clinical laboratories at the forefront of laboratory testing and diagnosis. The clinical specimens required for testing could have contained infectious agents that could cause disease in laboratory professionals if the exposure occurred during testing. During the Ebola outbreak of 2014, real and perceived concerns about instrument safety emerged and led laboratories to delay their testing – or refuse to test altogether.

Now, mainly because of the COVID-19 pandemic, our understanding of "clinical laboratories" has evolved to include testing in nursing homes, schools, shelters, correctional facilities, and parking lots. All of these settings could present biosafety risks to personnel. Therefore, we must broaden our application of biosafety, including guidance and training, to address all clinical testing locations.

In 2016, the Clinical Laboratory Improvement Advisory Committee (CLIAC), a federal advisory committee, issued the following recommendation:

CLIAC considers the matter of biosafety in clinical laboratories as an urgent, unmet national need. We, therefore, recommend that CDC convene a multidisciplinary task force to develop a biosafety strategy for clinical laboratories that:

- *Includes stakeholders from all areas of clinical laboratories (including professional societies), the diagnostic instrumentation industry, other relevant federal agencies, and patient/clinician representatives.*
- *Recommends areas requiring further research in clinical laboratory safety.*
- *Develops tools, templates, and guidelines for risk assessment in all areas of the clinical laboratories, both for routine operations and emerging infectious diseases.*
- *Publishes interim materials and progress reports broadly, and specifically to CLIAC, to inform and solicit input from the clinical laboratory and broader medical communities.*
- *Describes cultural, regulatory, measurement, and evaluation strategies for goal achievement in biosafety.*
- *Develops a framework for implementing good clinical practices that also address transparent evaluation and monitoring of biosafety practices.*

On June 24, 2022, CDC's Division of Laboratory Systems hosted the CDC Town Hall Meeting on Laboratory Biosafety – Use of Laboratory Instruments in collaboration with clinical and public health laboratory partners and instrument manufacturers. The purpose of this meeting was to provide an overview and discussion on laboratory biosafety when using laboratory instruments to test human and biological specimens. As a result of the town hall discussions, the CLIA program agencies, CDC, the Food and Drug Administration (FDA), and the Centers for Medicare & Medicaid Services (CMS) agreed to the formation of a new CLIAC workgroup to bring together the diagnostic instrument manufacturers, clinical and public health laboratory professionals, federal partners, and industrial hygienists to continue the discussions on biosafety issues with laboratory instrumentation revealed during the recent outbreaks and the pandemic.

CHARGE

The CLIAC Biosafety Workgroup is charged with providing input to CLIAC for consideration in making recommendations to the Department of Health and Human Services (HHS) on the potential additions to the CLIA regulations and the need for solutions that will improve the safety of laboratory professionals, their colleagues, and the environment.

DELIVERABLE

The output of the workgroup will be a summary report or periodic reports to CLIAC based on information gathered during meetings and discussions. The report will specifically address the priority topic areas and related questions. The workgroup Chair will present the reports at future CLIAC meetings for Committee deliberation and potential recommendations to HHS. The report may result in

CLIAC developing practical recommendations for potential solutions to address issues or gaps in laboratory instrumentation biosafety that may help improve outbreak and pandemic preparedness. The report may also result in CLIAC recommendations for HHS to consider for future rulemaking to update the CLIA regulations to ensure that laboratories are required to have policies and procedures addressing laboratory biosafety.

DISCUSSION QUESTIONS/THEMES

1) In vitro diagnostic product (IVD) instrument design plays a key role in mitigating biosafety issues that arise during routine use and maintenance schedules. How can interested parties better address biosafety for already established IVD instruments and IVD instruments currently under development?

a. What mechanisms/best practices do manufacturers currently use to assess biosafety considerations for established IVD instruments and IVD instruments currently under development?

i. Are there current mechanisms where end users can discuss/highlight biosafety issues with established IVD instruments within the end-user community and/or with the manufacturer? If so, what are they? How can manufacturers be included if they are currently not included?

ii. Are there mechanisms currently in place or that can be developed that would facilitate collaboration between manufacturers and a variety of clinical laboratory representatives during the use and maintenance of existing IVD instrumentation to incorporate or improve biosafety features?

b. When developing new IVD instrumentation, what considerations are typically given to biosafety with respect to instrument design (e.g., the robustness of instrument parts/materials to routine decontamination/sterilization procedures, use of disposable parts in areas of the instrumentation that are more at risk of contamination)?

c. Are there mechanisms currently in place or that can be developed that would facilitate collaboration between manufacturers and a variety of clinical laboratory representatives during the design stage for new IVD instrumentation under development to incorporate or improve biosafety features?

2) Laboratories receive and handle specimens that contain unknown pathogens on a routine basis. How can interested parties ensure proper biosafety activities for end users are established, effectively provided/communicated, and followed?

a. Are there widely available training materials for laboratory professionals that focus on instrument operation and cleaning and disinfection practices?

i. Do currently available biosafety training materials include sufficient information regarding instrument disinfection? If not, what minimum information should be included in these trainings?

b. Are there mechanisms in place or that can be developed by laboratories that would ensure annual biosafety training and/or competency assessment of laboratory staff?

3) What additions to the CLIA regulations could be made to ensure that laboratories are required to have policies and procedures addressing laboratory biosafety?

a. Currently, the Facilities standard at § 493.1101(d) indicates that “Safety procedures must be established, accessible, and observed to ensure protection from physical, chemical, biochemical, and electrical hazards, and biohazardous materials.” Should the CLIA regulations be updated to include additional safety standards as related to facilities that could include, but not be limited to, the items listed below?

- Proper workspace ventilation to safely handle contaminated specimens or pathogenic organisms at the appropriate biosafety level.
- Proper decontamination processes in place to help minimize contamination.
- Appropriate biosafety equipment and personal protective equipment available in accordance with the appropriate biosafety level.
- Requirement to report results of highly infectious organisms, potential agents of bioterrorism, and unusual multi-drug resistant organisms to State Public Health laboratories or CDC as required by Federal, State, or local government authority.

b. Currently, the General Considerations Standard at § 493.1804(a)(2) indicates that "To safeguard the general public against health and safety hazards that might result from laboratory activities." Should the CLIA regulations be updated to include additional safety standards related to General considerations?

4) Clear instructions and communication are key to addressing biosafety. Therefore,

a. How can manufacturers and clinical laboratories work together to provide clear, readily available biosafety instructions for each phase of testing, cleaning and disinfection practices, and maintenance of the instrument?

b. What resources are available for manufacturers to gain biosafety-related input to develop appropriate instructions (e.g., Environmental Protection Agency lists, Occupational Safety and Health Administration regulations)?

c. How can manufacturers gain input from biosafety professionals to aid the development of supplemental biosafety testing instructions for end users and service representatives?

d. How can non-regulatory organizations (e.g., the Clinical and Laboratory Standards Institute, the International Organization for Standardization), professional societies (e.g., The American Biological Safety Association, The American Society for Microbiology), and other interested parties assist in facilitating the process for manufacturers and laboratories?

Appendix B

CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC)
BIOSAFETY WORKGROUP ROSTER

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The CLIAC Next Generation Sequencing (NGS) Workgroup Report

CLIAC November 6, 2024

DR. NIRALI M. PATEL, WORKGROUP CHAIR

Background

- 2020 – CDC obtained public comment through a Request for Information (RFI) Concerning Personnel and the Retention of Next Generation Sequencing Data in Clinical and Public Health Laboratories, Docket CDC 2020-0051
- 2021 – CDC presented the NGS RFI summary report during the November 2021 CLIAC meeting
  - Recommendation: CLIAC recommends that CDC, CMS, and FDA convene a workgroup to define the scope of practice and the requisite CLIA qualifications for personnel performing bioinformatics data analysis and interpretation to produce test results that inform clinical decision-making.
- 2023 – Formation of the CLIAC NGS Workgroup
- 2024 – The NGS Workgroup met 4 times

Background

2020 – Request for Information (RFI) Concerning Personnel and the Retention of Next Generation Sequencing Data in Clinical and Public Health Laboratories

2021 – CDC presented the NGS RFI summary report during the November 2021 CLIAC meeting

2021 – CLIAC Recommendation to form the NGS Workgroup

2023 – Candidate recruitment and workgroup formation

2024 – Workgroup meetings and report to CLIAC

Workgroup Charge

The workgroup is charged with providing input to CLIAC for consideration in making recommendations to the Department of Health and Human Services on education, training, experience, and competencies that Clinical Laboratory Improvement Amendments of 1988 (CLIA) should require to qualify personnel performing next generation sequencing bioinformatic data analysis and interpretation.

Workgroup Members

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- Weiwei Zhang, MS, PhD

Workgroup Question

What are the current regulatory requirements and guidelines related to the role of bioinformatics in clinical and public health laboratories performing NGS?

Workgroup Discussion

- Bioinformatics pipelines are a critical component of the test system.
- The Health Insurance Portability and Accountability Act (HIPPA), the Health Information Technology for Economic and Clinical Health (HITECH) Act, the HIPAA Omnibus Rule, and cybersecurity requirements related to data privacy in bioinformatics activities must be considered.
- Staff performing bioinformatics activities under CLIA as testing personnel may not have expertise in all the roles discussed. Conversely, staff with expertise in infrastructure and development to run the pipeline may understand those biological pieces, but they might not have the qualifications that CLIA requires.
- The current CLIA regulations for personnel performing high complexity testing limit the ability to qualify bioinformaticians, as many do not have the biological science requirements. A carve-out for high complexity testing personnel performing bioinformatics may be needed.

Workgroup Question

Harmonization of definitions – Creating or defining the fields/terms used throughout workgroup discussions. Examples include:

- Health/Laboratory Informatics
- Bioinformatics
- Clinical Informatics
- Translational Informatics
- Informatician
- Bioinformatician

Workgroup Discussion

- There is a need to distinguish the bioinformatician from the informatician. The bioinformatician generated data related to the structure and function of biological systems. The informatician is more concerned with data related to patient care.
- Once CLIA-related activities are identified, roles can be defined, and educational requirements can be determined. Then the definitions can be developed and refined as related to those requirements.
- The workgroup members proposed a definition of bioinformation that includes an individual who manages, processes, and analyzes genomic and/or molecular data utilizing specialized software for the purposes of patient diagnosis or management.
- A broad definition/term should be used to avoid excluding groups needed for future laboratory needs. The term clinical laboratory informatician encompasses multiple roles related to NGS and may be more inclusive (e.g., bioinformatics and data science).

Workgroup Question

Workgroup discussion related to the education, training, experience, and competencies for various bioinformatics levels, including:

- An MS or PhD level individual who provides analytic leadership, tool selection, and database oversight.
- A bioinformatics technician who, for example, ensures data files are appropriately formatted for analysis, runs the analysis, and checks for the adequacy of the run.
- The skill sets required for the Laboratory Director (MD/DO or PhD) who carries overall responsibility for the clinical laboratory.

Workgroup Discussion

- The CLIA testing personnel qualifications for laboratories performing high-complexity testing should be modified to add an option to allow bioinformaticians to be qualified. The qualification paths may include specialized requirements for bioinformatics beyond biological sciences, including bioinformatics, genetics, statistics, computer science, software engineering, biochemistry, etc.
- There is a need for a carve-out to create a path for individuals who perform NGS or bioinformatics to qualify under CLIA, similar to how the current blood gas analysis carve-out is at § 493.1461 and § 493.1489. This carve-out should be developed for all CLIA-required personnel in the clinical laboratory.
- The workgroup members discussed the experience, responsibilities, and competencies that may be needed for bioinformaticians to qualify under CLIA.
- It is often the same person performing multiple roles, and discussions should focus on the work performed, skill sets needed, and education needed.
- The laboratory director and technical supervisors need to be knowledgeable on NGS and bioinformatics processes because they are the ones who are ultimately responsible. In addition to the current qualification requirements under CLIA, they should also have one year of training or experience in interpreting bioinformatics results.

Workgroup Question

Do the current CLIA regulations apply to the personnel discussed?

Workgroup Discussion

- The current CLIA regulations for personnel performing high complexity testing limit the ability to qualify bioinformaticians, as many do not have the biological science requirements.
- Personnel who develop the code and initial framework are not within the CLIA requirements.
- Personnel who implement and execute the code and use it on patients fall under CLIA.
- The existing CLIA personnel roles (testing personnel, general supervisor, technical supervisor, and director) can be used along with the experience and degree requirements as a framework to build upon.
- Workgroup members were asked to provide any recent job announcements or position descriptions to be used to develop draft qualifications and responsibilities.

Workgroup Agreements - General

The CLIA testing personnel qualifications for laboratories performing high complexity testing should be modified to add a qualification route and additional responsibilities for bioinformaticians.

- A CLIA personnel carve-out should be created to create a path for individuals who perform bioinformatics data analysis to qualify under CLIA, similar to how the current blood gas analysis carve-out is at § 493.1461 and § 493.1489. This carve-out should be developed for all CLIA-required personnel in the clinical laboratory who are involved in bioinformatics.
- The existing CLIA personnel roles (testing personnel, general supervisor, technical supervisor, and director) can be used along with the experience and degree requirements as a framework to build upon.

Workgroup Agreements - General

- The bioinformatician qualification paths may include specialized requirements for bioinformatics beyond biological sciences, including bioinformatics, genetics, statistics, computer science, software engineering, biochemistry, etc.
- A carve-out would also be needed for general supervisors, technical supervisors, and laboratory directors who oversee bioinformatics activities in laboratories performing high complexity testing using the workgroup's proposal for bioinformatics testing personnel as the baseline.

Workgroup Agreements -Definitions

- ***Bioinformatician*:** Individuals who manage, process, and analyze biological data utilizing specialized software.
- ***Bioinformatics*:** The interdisciplinary field that develops and applies computational methods to manage, process, and analyze biological data.
- ***Bioinformatics Pipeline*:** A set of multiple computer programs that may be run in series and/or in parallel to automate the process of analyzing biological data.

Workgroup Agreements - Qualifications

For a laboratory that performs bioinformatics, bioinformatics testing personnel must meet one of the following CLIA requirements:

- Meet the qualifications for testing personnel performing high complexity testing described at § 493.1489 (b)(1), (2), (3), (4), or (5) and have at least two years of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.
- Have earned a bachelor's, master's, or doctoral degree in bioinformatics, computational biology, computer science, mathematical science, or data science and have at least one year of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.
- Have education and training equivalency that includes at least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, includes 24 semester hours of science courses that include: (i) six (6) semester hours of chemistry or biology; and (ii) eighteen (18) semester hours of bioinformatics, computational biology, computer science, mathematical science, or data science in any combination and have at least one year of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.

Workgroup Agreements - Responsibilities

Each individual performs only those high complexity tests that are authorized by the laboratory director and require a degree of skill commensurate with the individual's education, training or experience, and technical abilities. Each individual performing high complexity testing must:

- *Develop and modify, as applicable, workflows, algorithms, and pipelines needed for clinical bioinformatics data analysis.
- *Conduct bioinformatics analysis, troubleshooting, and resolution.
- *Follow regulations and institutional policies related to the integrity, privacy, and security of patient and genomic data in databases and bioinformatics workflow processes throughout the testing process.

*_Note: New responsibilities that are not currently included in the CLIA regulations._

Thank you

CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC)
NEXT GENERATION SEQUENCING (NGS) WORKGROUP

MEETING SUMMARY REPORT

Workgroup Charge

The CLIAC NGS Workgroup is charged with providing advice to CLIAC for consideration in making recommendations to the Department of Health and Human Services (HHS) on education, training, experience, and competencies that should be required by CLIA to qualify personnel performing next generation sequencing bioinformatics data analysis and interpretation.

Workgroup Agreements

The CLIA testing personnel qualifications for laboratories performing high complexity testing should be modified to add a qualification route and additional responsibilities for bioinformaticians.

- A CLIA personnel carve-out should be created to create a path for individuals who perform bioinformatics data analysis to qualify under CLIA, similar to how the current blood gas analysis carve-out is at § 493.1461 and § 493.1489. This carve-out should be developed for all CLIA-required personnel in the clinical laboratory who are involved in bioinformatics.
- The existing CLIA personnel roles (testing personnel, general supervisor, technical supervisor, and director) can be used along with the experience and degree requirements as a framework to build upon. For example, a bachelor's degree plus four years of experience or a PhD plus six months of experience.
- The bioinformatician qualification paths may include specialized requirements for bioinformatics beyond biological sciences, including bioinformatics, genetics, statistics, computer science, software engineering, biochemistry, etc.
- A carve-out would also be needed for general supervisors, technical supervisors, and laboratory directors who oversee bioinformatics activities in laboratories performing high complexity testing using the workgroup's proposal for bioinformatics testing personnel as the baseline.

The workgroup agreed upon the following definitions, qualifications, and responsibilities that can be used to develop a carve-out in the CLIA regulations for bioinformatics testing personnel in laboratories performing high complexity testing.

Definitions

- *Bioinformatician:* Individuals who manage, process, and analyze biological data utilizing specialized software.
- *Bioinformatics:* The interdisciplinary field that develops and applies computational methods to manage, process, and analyze biological data.
- *Bioinformatics Pipeline:* A set of multiple computer programs that may be run in series and/or in parallel to automate the process of analyzing biological data.

Bioinformatician Qualifications

Bioinformaticians in laboratories performing high complexity testing must possess a current license issued by the state in which the laboratory is located if such licensing is required. In addition, bioinformaticians can qualify as testing personnel by meeting one of the requirements listed below.

For a laboratory that performs bioinformatics, bioinformatics testing personnel must meet one of the following CLIA requirements:

- Meet the qualifications for testing personnel performing high complexity testing described at § 493.1489 (b)(1), (2), (3), (4), or (5) and have at least two years of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.
- Have earned a bachelor's, master's, or doctoral degree in bioinformatics, computational biology, computer science, mathematical science, or data science and have at least one year of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.
- Have education and training equivalency that includes at least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, includes 24 semester hours of science courses that include: (i) six (6) semester hours of chemistry or biology; and (ii) eighteen (18) semester hours of bioinformatics, computational biology, computer science, mathematical science, or data science in any combination and have at least one year of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.

Bioinformatician Responsibilities

Bioinformaticians are responsible for managing, processing, and analyzing genomic and/or molecular data utilizing specialized software for the purposes of patient diagnosis or management.

Each individual performs only those high complexity tests that are authorized by the laboratory director and require a degree of skill commensurate with the individual's education, training or experience, and technical abilities. Each individual performing high complexity testing must:

- Follow the laboratory's procedures for specimen handling and processing, test analyses, reporting, and maintaining records of patient test results.
- Maintain records that demonstrate that proficiency testing samples are tested in the same manner as patient specimens.
- Adhere to the laboratory's quality control policies and document all quality control activities, instrument and procedural calibrations, and maintenance performed.
- Follow the laboratory's established policies and procedures whenever test systems are not within the laboratory's established acceptable levels of performance.
- Be capable of identifying problems that may adversely affect test performance or reporting of test results, and either must correct the problems or immediately notify the general supervisor, technical supervisor, clinical consultant, or director.
- Document all corrective actions taken when test systems deviate from the laboratory's established performance specifications.
- *Develop and modify, as applicable, workflows, algorithms, and pipelines needed for clinical bioinformatics data analysis.
- *Conduct bioinformatics analysis, troubleshooting, and resolution.
- *Follow regulations and institutional policies related to the integrity, privacy, and security of patient and genomic data in databases and bioinformatics workflow processes throughout the testing process.

**Note: New draft responsibilities are not currently included in the CLIA regulations.*

Meeting #1 Summary – March 15, 2024

1. **What are the current regulatory requirements and guidelines related to the role of bioinformatics in clinical and public health laboratories performing NGS?**

   Workgroup Discussion and Comments

   - To set the stage for discussion, Ms. Penny Keller the workgroup's CMS ex officio, provided a presentation on the Clinical Laboratory Improvement Amendments of 1988 (CLIA) Fees, Histocompatibility, Personnel, and Alternative Sanctions for Certificate of Waiver Laboratories Final Rule published in the Federal Register on December 28, 2023.
   - Individuals who run a lockdown pipeline will have different expertise, training, and backgrounds than those who need to develop it, assess it, and know what tools are needed to achieve the best scientific outcomes and data analysis.
   - Staff performing bioinformatics activities under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as testing personnel may not have expertise in all the roles discussed. Conversely, staff with expertise in infrastructure and development to run the pipeline may understand those biological pieces, but they might not have the qualifications that CLIA requires.
   - When determining roles under CLIA, the test system and the activities considered for research and development versus those that are part of the clinical test need to be considered.
   - Bioinformatics pipelines are a critical component of the test system.
   - The Health Insurance Portability and Accountability Act (HIPPA), the Health Information Technology for Economic and Clinical Health (HITECH) Act, the HIPAA Omnibus Rule, and cybersecurity requirements related to data privacy in bioinformatics activities must be considered.
   - The current CLIA regulations for personnel performing high complexity testing limit the ability to qualify bioinformaticians, as many do not have the biological science requirements. A carve-out for high complexity testing personnel performing bioinformatics may be needed.
   - Laboratories may utilize third-party companies and services that build and validate the bioinformatics pipeline and return the results to the laboratory but do not have a CLIA certificate.
   - Workgroup members discussed the practice of bioinformatics. Several members suggested dividing the activities into categories with responsibilities and qualifications associated with the roles and noted that often, the same person performs multiple roles.
     1. Pipeline Development and Maintenance
        - Responsibilities
          - Developing, coding, putting it into management workflows, doing many infrastructure pieces, and developing pipelines.
          - Need to understand the biological aspects of what it means to have a different trimming tool and how that will impact some of those downstream variant calls just because of the stringency of the trimming. They need to know how to evaluate those pieces in the context of clinical diagnostics.
          - Serve as backup for bioinformaticians doing the day-to-day work so they know when updates are needed, identify gaps in pipelines, or identify points that need to be optimized or improved to streamline the process.
        - Qualifications
          - Bioinformatics master's or Bioinformatics PhD

- Bachelor's degree in biological science, computational related field, computer science, engineering
- One year of training/experience preferred but not required for entry-level

2. Bioinformaticians
   - Responsibilities
     - Build new tools, libraries, pipelines, databases, data visualizations, dashboards, report templates, Laboratory Information Management System (LIMS)/Electronic Laboratory Reporting (ELR) and electronic health record (EHR) integration, etc.
     - Handle data and run predefined tools, scripts, and pipelines
     - Download sequencing files
     - Conduct routine quality control (QC) and performance monitoring
     - Monitor effectiveness and potential problems over time
     - Resolving issues, such as restarting pipelines manually when errors occur
     - Updating pipelines with new versions of external software updates
     - Upload to LIMS
     - Perform data aggregation
     - Generate reports
     - Report out or share information with interested parties
   - Qualifications
     - MS or PhD in one of the following areas: Computer Science, Bioinformatics, Computer Engineering, Genetics/Genomics, Computational Biology
     - PhD with one year of supervisory experience or an MS with two years of training and experience,
     - The CLIA Laboratory Director should have an additional year of training or experience in interpreting bioinformatics results
3. Data Aggregation/Data Mining/Data Extraction
   - Responsibilities
     - Bioinformatician who will go back and pull data and perform some data visualization.
     - Monitor effectiveness and identification of potential problems over time

2. Harmonization of definitions – Creating or defining the fields/terms used throughout workgroup discussions. Examples include:

- **Health/Laboratory Informatics**
- **Bioinformatics**
- **Clinical Informatics**
- **Translational Informatics**
- **Informatician**
- **Bioinformatician**

Workgroup Discussion and Comments

- The workgroup used the Centers for Disease Control and Prevention (CDC) Request for Information (RFI)**:** personnel and the retention of next generation sequencing data in clinical and public health laboratories (Docket CDC 2020-0051) summary report as a guide for discussing definitions.
- There is a need to distinguish the bioinformatician from the informatician. The bioinformatician generated data related to the structure and function of biological systems. The informatician is more concerned with data related to patient care.

- Once CLIA-related activities are identified, roles can be defined, and educational requirements can be determined.
- Members discussed if the development of the NGS bioinformatics pipeline itself was a CLIA-related activity that needed to have CLIA-required testing personnel.
  - Commercially purchased bioinformatics pipelines and tools may not require having developers under CLIA.
  - Developers should work with the laboratory to develop and establish key thresholds and QC parameters.
  - Developers who are integral to the laboratory processes as laboratories establish performance specifications and perform validation of the bioinformatics pipelines should be CLIA-required testing personnel.
- The impact of clinical testing and testing results should be considered when determining if staff should be qualified under CLIA.
- The laboratory director and technical supervisors need to be knowledgeable on NGS and bioinformatics processes because they are the ones who are ultimately responsible. In addition to the current qualification requirements under CLIA, they should also have one year of training or experience in interpreting bioinformatics results.
- The workgroup discussed removing informaticians from the list of definitions as their roles are not typically related to CLIA activities.
- It is often the same person performing multiple roles, and discussions should focus on the work performed, skill sets needed, and education needed.
- Members noted that qualifying individuals to serve as technical supervisors in laboratories performing NGS is difficult since the current CLIA regulations focus on biological degrees. There is a need to expand CLIA to include genetics or statistics, along with experience in clinical laboratory bioinformatics.
- The CLIA testing personnel qualifications for laboratories performing high-complexity testing should be modified to add an option to allow bioinformaticians to be qualified. The qualification paths may include specialized requirements for bioinformatics beyond biological sciences, including bioinformatics, genetics, statistics, computer science, software engineering, biochemistry, etc.
- There is a need for a carve-out to create a path for individuals who perform NGS or bioinformatics to qualify under CLIA, similar to how the current blood gas analysis carve-out is at § 493.1461 and § 493.1489. This carve-out should be developed for all CLIA-required personnel in the clinical laboratory.
- Professional organizations such as the Association for Molecular Pathology (AMP) are involved in these discussions and may be a source for additional information.

Meeting #2 Summary – April 26, 2024

1. **Workgroup discussion education, training, experience, and competencies for various bioinformatics levels, including:**
   - **An MS or PhD level individual who provides analytic leadership, tool selection, and database oversight.**
   - **A bioinformatics technician who, for example, ensures data files are appropriately formatted for analysis, runs the analysis, and checks for the adequacy of the run.**
   - **The skill sets required for the Laboratory Director (MD/DO or PhD) who carries overall responsibility for the clinical laboratory.**

Workgroup Discussion and Comments

- The workgroup members proposed a definition of bioinformatician that includes an individual who manages, processes, and analyzes genomic and/or molecular data utilizing specialized software for the purposes of patient diagnosis or management.
- The current CLIA personnel qualifications and responsibilities framework should be utilized to develop a carve-out for bioinformaticians.
- A broad definition/term should be used to avoid excluding groups needed for future laboratory needs. The term clinical laboratory informatician encompasses multiple roles related to NGS and may be more inclusive (e.g., bioinformatics and data science).
- The roles within the CLIA test system (pre-analytical, analytical, and post-analytical) should be considered, along with distinguishing between clinical bioinformatics, research and development, and other bioinformatics roles.
- There is a need to allow delegation of certain tasks related to NGS to other personnel.
- The workgroup members discussed the qualifications required for bioinformaticians, including:
    - Master's or PhD in bioinformatics, biostatistics, computer science, data science, mathematics, computer engineering, genetics/genomics, computational biology, or similar field
    - Bachelor's degree in bioinformatics can qualify as testing personnel
    - Bachelor's degree in biology or biological sciences
    - Certifications from a formal academic program are acceptable without a degree
    - UCSD certification: https://extendedstudies.ucsd.edu/courses-and-programs/applied-bioinformatics
    - UCSD BS in Bioinformatics Course: https://biology.ucsd.edu/education/undergrad/maj-min/majors/fall20-later/bioinformatics.html
- Competencies that may be required for bioinformaticians include:
    - Database skills, coding, mining, storage, deployment, genetics, data science, technical proficiency skills, IT, algorithm, and model development
    - Data management, data security, and privacy, cybersecurity, HIPAA, CLIA, QC
- Cybersecurity and HIPAA training are needed for individuals to have the same baseline understanding and language while interacting with clinical workflows.
- The workgroup members discussed the experiences needed for bioinformaticians to qualify under CLIA, including:
    - Bachelor's degree with one year of training/experience preferred but not required for entry-level
    - Master's degree with two years of training and experience
    - PhD should have at least one year of supervisory experience
    - Clinical experience, CLIA, coding, IT, and genetics is desired
    - Testing personnel should have six months or one year of experience in a laboratory or performing analyses
    - Use the current CLIA lab director requirements and add one year of training or experience in interpreting bioinformatics results as a requirement
    - Laboratory directors and general supervisors have a certain level of knowledge, proficiency, and competency in bioinformatics.
- The workgroup members provided a list of bioinformatician roles and responsibilities that include:
    - Writing code and programming for the informatics pipeline
    - Validation of pipelines, revalidation, and development of reports
    - Checking runs, troubleshooting, modifying run sheets or parameters
    - Understanding CLIA roles and regulations

- Operate QC/testing or clinical QC
- Code development (Does not fall under the CLIA requirements)
- Implementing and executing the code (Falls under CLIA requirements)
- Large data manipulation, data management, analysis, proteomics, methylation
- Streamline and scale production
- Oversee the bioinformatics activities, especially in the wet lab (e.g., clinically vet and review code)
- Bioinformatics and IT roles: IT is responsible for activities in production-level environments. IT partners with bioinformatics to develop and automate long-term codes.

2. **Do the current CLIA regulations apply to the personnel discussed?**

Workgroup Discussion and Comments

- Personnel who implement and execute the code and use it on patients fall under CLIA.
- Personnel who develop the code and initial framework are not within the CLIA requirements.
- Individuals with a biology degree qualify as CLIA testing personnel.
- The existing CLIA personnel roles (testing personnel, general supervisor, technical supervisor, and director) can be used along with the experience and degree requirements as a framework to build upon. For example, a bachelor's degree plus four years of experience or a PhD plus six months of experience.
- Workgroup members were asked to provide any recent job announcements or position descriptions to be used to develop draft qualifications and responsibilities for presentation during the next meeting.

Meeting #3 Summary – August 30, 2024

CDC workgroup staff used the previous workgroup meeting transcripts and the position descriptions provided by workgroup members to develop a summary (see Appendix A). From the summary, draft definitions, qualifications, and responsibilities for testing personnel in a laboratory performing high complexity testing were created and provided for workgroup member discussion and refinement. The first draft provided to the workgroup for discussion during the August 30, 2024, meeting is provided below.

DRAFT - Definitions

- *Bioinformatician:* Individuals who manage, process, and analyze genomic and/or molecular data utilizing specialized software for the purposes of patient diagnosis or management.
- *Bioinformatics:* The interdisciplinary field that develops and applies computational methods to analyze biological data, particularly large-scale datasets generated by genomic and proteomic experiments.
- *Next Generation Sequencing (NGS):* A high-throughput methodology that enables rapid sequencing of large segments of DNA or entire genomes.
- *Computational Pipeline:* A series of computational steps that automate the process of analyzing and interpreting biological data.

DRAFT - Bioinformatician Qualifications

Bioinformaticians in laboratories performing high complexity testing must possess a current license issued by the state in which the laboratory is located if such licensing is required. In addition, bioinformaticians can qualify as testing personnel by meeting one of the requirements listed below.

For a laboratory that performs bioinformatics, testing personnel must meet one of the following CLIA requirements:

- Meet the qualifications for testing personnel performing high complexity testing described at § 493.1489 (b)(1), (2), (3), (4), or (5).
- Have earned a bachelor's degree in bioinformatics, computer sciences, or computational biology, and have at least three months of documented laboratory training performing bioinformatics analysis in a laboratory performing high complexity testing.
- Have education and training equivalency that includes at least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, includes 24 semester hours of science courses that include (i) six (6) semester hours of chemistry or biology; (ii) six (6) semester hours of computer sciences; and (iii) twelve (12) semester hours of bioinformatics, computer sciences, mathematical sciences, or computational biology in any combination and have at least three months of documented laboratory training performing bioinformatics analysis in a laboratory performing high complexity testing.

DRAFT - Bioinformatician Responsibilities

Bioinformaticians are responsible for managing, processing, and analyzing genomic and/or molecular data utilizing specialized software for the purposes of patient diagnosis or management.

Each individual performs only those high complexity tests that are authorized by the laboratory director and require a degree of skill commensurate with the individual's education, training or experience, and technical abilities. Each individual performing high complexity testing must:

- Follow the laboratory's procedures for specimen handling and processing, test analyses, reporting, and maintaining records of patient test results.
- Maintain records that demonstrate that proficiency testing samples are tested in the same manner as patient specimens.
- Adhere to the laboratory's quality control policies and document all quality control activities, instrument and procedural calibrations, and maintenance performed.
- Follow the laboratory's established policies and procedures whenever test systems are not within the laboratory's established acceptable levels of performance.
- *Develop tools and/or algorithms and/or modify pipelines needed for genomic analysis.
- *Conduct bioinformatics analysis, troubleshooting, and resolution.
- *Maintain security measures for results and patient-specific data electronically shared through networked or other interfaced systems throughout the testing process.
- Be capable of identifying problems that may adversely affect test performance or reporting of test results, and either must correct the problems or immediately notify the general supervisor, technical supervisor, clinical consultant, or director.
- Document all corrective actions taken when test systems deviate from the laboratory's established performance specifications.

*Note: New draft responsibilities are not currently included in the CLIA regulations.

Workgroup Discussion and Comments

- The summarized information provides a draft for testing personnel performing bioinformatic activities. However, a carve-out would also be needed for general supervisors, technical supervisors, and laboratory directors who oversee bioinformatic activities in laboratories performing high complexity testing.

- Workgroup members suggested expanding the degree qualifications to include data science, statistics, mathematics, or related fields. Other members suggested information technology or engineering degrees.
- Three or six months of laboratory training or experience performing clinical bioinformatic analysis in a laboratory performing high complexity testing is needed for each qualification path. Many workgroup members felt three months was insufficient time for proper training and experience. The current CLIA regulations indicate that testing personnel who qualify using the education equivalence path must have laboratory training that includes at least three months of documented laboratory training in each specialty in which the individual performs high complexity testing. Therefore, the three month requirement is aligned with the current CLIA requirements.
- There may be a need to include certification requirements.
- It may be clearer to indicate six semester hours of biology or chemistry and 18 semester hours of the other disciplines.
- One member suggested that expanding the applicant pool for bioinformatics testing personnel under CLIA regulations could involve recognizing other relevant training and educational backgrounds that are not strictly limited to the fields of bioinformatics, computer sciences, or computational biology and provided the following suggestions:
    - Biotechnology or Molecular Biology Degrees: Graduates with degrees in biotechnology or molecular biology often have a strong background in laboratory techniques, genetics, and data analysis, which are crucial for bioinformatics roles. Supplementing this with targeted bioinformatics training or certification could make them eligible.
    - Medical Laboratory Science (MLS) Degrees: Individuals with a background in medical laboratory science may already have experience with high-complexity testing. By acquiring additional training in bioinformatics, they could meet the qualifications for bioinformatics testing personnel.
    - Statistics or Biostatistics Degrees: Statistics or biostatistics graduates possess strong analytical and data interpretation skills. They could be well-suited for these roles with additional coursework or certifications in bioinformatics or computational biology.
    - Genomics or Genetics Degrees: Degrees focused on genomics or genetics often include bioinformatics and data analysis components. Candidates from these fields could meet the requirements with additional training in computational techniques and bioinformatics software.
    - Engineering Degrees with a Focus on Bioengineering or Computational Biology: Bioengineers or those with a background in computational biology within engineering programs often possess relevant skills in both biological sciences and computational methods, making them strong candidates after some focused laboratory training.
    - Health Informatics or Biomedical Informatics Degrees: Individuals with degrees in health informatics or biomedical informatics are trained in managing and analyzing large sets of health-related data. With specialized training in bioinformatics, they could contribute to bioinformatics testing personnel roles.
    - Mathematics or Applied Mathematics Degrees with Bioinformatics Focus: Those with a background in mathematics or applied mathematics who have taken bioinformatics-related courses or have completed projects in computational biology could be trained to meet the specific requirements for high-complexity testing.
    - Post-Baccalaureate Certificates or Professional Certifications: Offering post-baccalaureate certificates or professional certifications in bioinformatics, computational biology, or laboratory analysis could help individuals from related fields gain the required qualifications.

    - Apprenticeship Programs: Establishing apprenticeship or internship programs that offer hands-on bioinformatics analysis in laboratories performing high-complexity testing could provide the required training for individuals from diverse educational backgrounds.
    - On-the-Job Training Programs: Developing structured on-the-job training programs within clinical laboratories that allow individuals with relevant degrees to gain experience in bioinformatics could help meet the CLIA requirements while expanding the candidate pool.
- By broadening the recognized educational backgrounds and providing structured pathways for additional training, the applicant pool for bioinformatics testing personnel can be significantly expanded while still maintaining the necessary competencies for high complexity testing.
- Members commented that the third new responsibility may be too focused on IT and not specific to bioinformatics. Others noted that maintaining security measures should be part of the responsibility to ensure secure access to patient information.
- It was suggested that the first new responsibility be broadened to include workflows and pipelines for bioinformatic data analysis.
- The workgroup discussed and refined the draft definitions, assuming that they would apply to clinical laboratory testing under CLIA.

Meeting #4 Summary – October 18, 2024

The draft definitions, qualifications, and responsibilities for testing personnel in a laboratory performing high complexity testing were updated based on the discussions from the August 30, 2024, meeting. The updated draft is provided below and was discussed and refined during the October 18, 2024, workgroup meeting.

DRAFT 2 - Definitions

- *Bioinformatician:* Individuals who manage, process, and analyze biological data utilizing specialized software.
- *Bioinformatics:* The interdisciplinary field that develops and applies computational methods to manage, process, and analyze biological data.
- *Next Generation Sequencing (NGS):* A high-throughput methodology that enables rapid sequencing of large segments of DNA or entire genomes.
- *Bioinformatic Pipeline:* A set of multiple computer programs that may be run in series and/or in parallel to automate the process of analyzing and interpreting biological data.

DRAFT 2 - Bioinformatician Qualifications

Bioinformaticians in laboratories performing high complexity testing must possess a current license issued by the state in which the laboratory is located if such licensing is required. In addition, bioinformaticians can qualify as testing personnel by meeting one of the requirements listed below.

For a laboratory that performs bioinformatics, testing personnel must meet one of the following CLIA requirements:

- Meet the qualifications for testing personnel performing high complexity testing described at § 493.1489 (b)(1), (2), (3), (4), or (5) and have at least *3 or 6 months* of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.
- Have earned a bachelor's, master's, or doctoral degree in bioinformatics, computational biology, computer science, mathematical science, or data science and have at least *3 or 6 months* of

documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.

- Have education and training equivalency that includes at least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, includes 24 semester hours of science courses that include: (i) six (6) semester hours of chemistry or biology; and (ii) eighteen (18) semester hours of bioinformatics, computational biology, computer science, mathematical science, or data science in any combination and have at least *3 or 6 months* of documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing.

DRAFT 2 - Bioinformatician Responsibilities

Bioinformaticians are responsible for managing, processing, and analyzing genomic and/or molecular data utilizing specialized software for the purposes of patient diagnosis or management.

Each individual performs only those high complexity tests that are authorized by the laboratory director and require a degree of skill commensurate with the individual's education, training or experience, and technical abilities. Each individual performing high complexity testing must:

- Follow the laboratory's procedures for specimen handling and processing, test analyses, reporting, and maintaining records of patient test results.
- Maintain records that demonstrate that proficiency testing samples are tested in the same manner as patient specimens.
- Adhere to the laboratory's quality control policies and document all quality control activities, instrument and procedural calibrations, and maintenance performed.
- Follow the laboratory's established policies and procedures whenever test systems are not within the laboratory's established acceptable levels of performance.
- *Develop and modify, as applicable, workflows, algorithms, and pipelines needed for clinical bioinformatics data analysis.
- *Conduct bioinformatics analysis, troubleshooting, and resolution.
- **Ensure/Adhere to/Follow* regulatory and organizational integrity, privacy, and security of patient and genomic data in databases and bioinformatics workflow processes throughout the testing process.
- Be capable of identifying problems that may adversely affect test performance or reporting of test results, and either must correct the problems or immediately notify the general supervisor, technical supervisor, clinical consultant, or director.
- Document all corrective actions taken when test systems deviate from the laboratory's established performance specifications.

*Note: New draft responsibilities are not currently included in the CLIA regulations.

Workgroup Discussion and Comments

- Members suggested that there was no need to define NGS since it is not included in the bioinformatics personnel qualifications and responsibilities workgroup agreements.
- A suggestion was made to remove data interpretation from the bioinformatics pipeline definition, as interpretation may be associated with the practice of medicine.
- Members discussed the suggested requirement for documented laboratory training performing clinical bioinformatics analysis in a laboratory performing high complexity testing and emphasized the need for a longer requirement for training due to the complexities of the bioinformatics activities. Members agreed that for individuals with bioinformatics education or education equivalency, at least one year should be required. On the other hand, individuals

meeting the current testing personnel qualifications for high-complexity testing may need additional training, which is suggested to be two years.

- Members finalized the workgroup agreements that will be included in the presentation to CLIAC during the November 6-7, 2024, meeting.

Resources

1. Clinical Laboratory Improvement Amendments of 1988 (CLIA) Fees, Histocompatibility, Personnel, and Alternative Sanctions final rule (CMS-3326-F).
2. The Centers for Disease Control and Prevention (CDC) Request for Information: Personnel and the Retention of Next Generation Sequencing Data in Clinical and Public Health Laboratories, Docket CDC 2020-0051, summary report. https://www.cdc.gov/cliac/docs/november-2021/8a_CDC-NGS-RFI_Comment-Analysis-Report.pdf
3. The Next Generation Sequencing Quality Initiative
4. The NGS Quality Initiative Bioinformatician Competency Assessment Standard Operating Procedure and Bioinformatician Competency Assessment Summary Form.

Appendix A

CLIAC Next Generation Sequencing Workgroup: Summary of Meeting Transcripts and Position Descriptions

Determining Qualifications of a Bioinformatician or Someone Performing Bioinformatics

Summary of Workgroup Meeting Transcripts and Position Descriptions Provided by Workgroup Members

The educational requirements of candidates are typically similar across all institutions as they provide information about the qualifications and experience required for a bioinformatician position. However, the level of education, years of experience, and training will vary depending on whether the position is entry-level. Across multiple institutions, the similarities include the requirement of a degree (e.g., bachelor's, master's, or doctoral) in subjects such as Bioinformatics, Computational Biology, Computer Science, Computer Engineering, Microbiology, Biology, Molecular Biology, Biomedical Sciences, Genetics, Genomics, Virology, Parasitology, Evolutionary Biology, Biostatistics, Genetic Counseling (Master's level), Mathematical Sciences (and related disciplines), Digital Health, or a related field. Few institutions identified degree requirements outside of these, i.e., associate degree, vocational, certificate(s), or otherwise. Across institutions, differences lie in the specific requirements for years of experience and additional educational qualifications. Some institutions mention a preference for candidates with a master's degree or PhD in a specific area of study, while others specify the number of years of experience required. The average number of years of experience varies across the institutions. Some summaries mention a requirement of 2 or more years of experience without a PhD, while others state that none or one year of experience is required with a PhD. Additionally, some institutions may provide additional information about preferred experience or expertise in certain areas within bioinformatics or computational biology.

Some institutions identified the need to divide bioinformatics-related duties among three levels of personnel performing bioinformatics. The workgroup may consider how these requirements vary as applicable to these three levels summarized:

1. Junior—The Junior Bioinformatician will support the bioinformatics team in performing computational analysis on genomic data using established tools under supervision. This role focuses on learning best practices in data analysis while contributing to ongoing research projects.
    a. Duties could include assisting in running established bioinformatics pipelines for NGS data analysis, performing basic quality control checks on sequencing data, helping maintain databases and manage data storage solutions under guidance, developing proficiency in programming languages used within the team (e.g., Python, C++, Visual Basic, C#, etc.), participating in team meetings and contributing to discussions on project progress.
    b. Qualifications could include a bachelor's degree in bioinformatics, computational biology, or a related field, familiarity with the Linux environment and command-line tools, and a basic understanding of genomics and molecular biology concepts.
2. Mid-level - The Mid-Level Bioinformatician will independently conduct bioinformatics analyses and contribute to developing new computational pipelines. This role requires a solid understanding of genomics and strong analytical skills to support both research initiatives and clinical applications.

    a. Duties include designing, testing, and implementing custom bioinformatics pipelines for complex datasets and providing insights into pipeline optimization based on the latest scientific literature. Collaborating with laboratory personnel to align sequencing protocols with bioinformatics requirements, contributing to manuscript preparation, and presenting findings at scientific meetings.
    b. Qualifications could include a master's degree in bioinformatics or a related field or a bachelor's degree with 2+ years' experience in a relevant area. Proficiency with programming languages such as Python, C++, Visual Basic, C#, etc.; experience with Unix/Linux environments; familiarity with version control systems like GitHub.
3. Senior - The Senior Bioinformatician leads the development of advanced computational strategies for large-scale genomic analyses that drive research innovation and clinical decision-making processes.
    a. Duties include leading the design and implementation of robust computational pipelines across various projects within an organization or institution, overseeing quality assurance/control processes to ensure the accuracy of genomic analyses, and setting standards for best practices within the team or department. Mentoring junior members, providing training on advanced techniques in bioinformatics analysis, and fostering an environment conducive to collaborative research efforts across disciplines. Drives strategic planning efforts by staying ahead of emerging trends within genomics. They advise leadership on how to integrate cutting-edge technologies into organizational workflows.
    b. Qualifications include a PhD in Bioinformatics, Computational Biology, or a related field preferred or a master's degree with significant experience (5+ years) leading complex projects within a bioinformatics context. Demonstrated expertise in developing novel algorithms/tools for genome assembly, annotation, variant calling, etc.; extensive knowledge working with cloud computing environments; strong publication record indicative of impactful contributions to the field.

Essential Duties and Competencies of a Bioinformatician or Someone Performing Bioinformatics

Essential Job Duties Summarized from Workgroup Meeting Transcripts and Position Descriptions Provided by Workgroup Members:

Each entity outlines the specific responsibilities and tasks associated with a bioinformatician or similar position. These responsibilities typically include maintaining quality assurance/control of data, developing tools and/or algorithms for genomic analysis, conducting bioinformatics analysis, developing pipelines, troubleshooting and resolution, educating/training staff (bioinformaticians and non-bioinformaticians), guiding policy development or contributing to strategic planning efforts, and summarizing/communicating results (including result reporting). The differences lie in the specific details and emphasis on certain responsibilities based on the organization's or institution's needs and priorities. Some institutions provide more specific examples or additional responsibilities. For example, some institutions have identified requirements for maintaining up-to-date knowledge on emerging technologies and scientific advancements in the field of genomics and bioinformatics, ensuring compliance with data privacy standards when handling sensitive patient information (e.g., HIPAA compliance), and participating in grant writing activities to secure funding for research projects, prior knowledge of clinical/public health laboratory guidelines and regulations, usage of specific tools, scripts, and/or pipelines, familiarity with Laboratory Information Management System (LIMS)/Electronic

Laboratory Reporting (ELR), and electronic health record (EHR) integration, and specific duties regarding data management, data security, and data mining.

Candidate Skills and Characteristics Summarized from Workgroup Meeting Transcripts and Position Descriptions Provided by Workgroup Members:
Required skills and characteristics highlight the additional knowledge and skills required for the Bioinformatics Scientist position. These typically include a deep understanding of genomics and molecular biology, experience analyzing large sequencing datasets, proficiency in programming languages (such as Python), familiarity with Linux/Unix environments, and strong communication skills. The differences lie in the specific technical requirements mentioned, such as working within a High-Performance Computing infrastructure, cloud-based data storage, and analytics interfaces, or experience with version control tools. Additionally, some institutions may mention preferences for expertise in specific lab settings (such as CAP/CLIA and bioinformatics specific to clinical or public health settings), ability to obtain security clearances or specific certifications, knowledge of and compliance with the HIPAA Final Security Rule, HITECH, GINA and HIPAA Omnibus regulatory requirements and project management knowledge/experience.

Competencies Summarized from Workgroup Meeting Transcripts and Position Descriptions Provided by Workgroup Members:
Competencies for Bioinformatician positions are similar across all institutions as they focus on the specific responsibilities related to data quality assessment and data analysis in the context of bioinformatics. These responsibilities typically include coding bioinformatics analysis computer programs, assessing the quality of sequencing data, implementing quality control measures, evaluating the sensitivity and specificity of bioinformatics analysis results, developing evaluation plans, selecting appropriate data for testing, and utilizing data visualization tools. Institutional differences lie in the specific details and emphasis placed on certain responsibilities based on the organization's or institution's needs and priorities. Some institutions may provide more specific examples or additional responsibilities, and a few have identified additional needs, such as the ability to interrogate big data.

Appendix B

Testing Personnel Qualifications § 493.1489 effective December 28, 2024

Testing personnel in laboratories performing high complexity testing must possess a current license issued by the state in which the laboratory is located if such licensing is required. In addition, testing personnel can qualify by meeting one of the routes listed below.

- Be a doctor of medicine, doctor of osteopathy, or doctor of podiatric medicine licensed to practice medicine, osteopathy, or podiatry in the state in which the laboratory is located.
- Have earned a doctoral, master's, or bachelor's degree in a chemical, biological, clinical, or medical laboratory science, or medical technology from an accredited institution.
- Meet the qualification requirements for laboratory director at § 493.1443(b)(3) or technical supervisor at §493.1449(c)(4) or (5). Qualification routes under this pathway include:
  - Hold an earned doctoral degree and have at least 16 semester hours of doctoral-level coursework in biology, chemistry, medical technology (MT), clinical laboratory science (CLS), or medical laboratory science (MLS).
  - Hold an earned doctoral degree and have an approved thesis or research project in biology/chemistry/MT/CLS/MLS related to laboratory testing for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings.
  - Have earned a master's degree in chemical, biological, clinical, or medical laboratory science, or medical technology from an accredited institution.
  - Meet bachelor's degree equivalency and have at least 16 semester hours of additional graduate-level coursework in chemical, biological, clinical, or medical laboratory science, or medical technology.
  - Meet bachelor's degree equivalency and have at least 16 semester hours in a combination of graduate level coursework in biology, chemistry, medical technology, or clinical or medical laboratory science and an approved thesis or research project related to laboratory testing for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings.
  - Have earned a bachelor's degree in chemical, biological, clinical, or medical laboratory science, or medical technology from an accredited institution.
  - Have at least 120 semester hours, or equivalent, from an accredited institution that, at a minimum, includes forty-eight (48) semester hours of medical laboratory technology courses.
  - Have at least 120 semester hours, or equivalent, from an accredited institution that, at a minimum, includes forty-eight (48) semester hours of science courses that include: (i) twelve (12) semester hours of chemistry, which must include general chemistry and biochemistry or organic chemistry; (ii) twelve (12) semester hours of biology, which must include general biology and molecular biology, cell biology or genetics; and (iii) twenty-four (24) semester hours of chemistry, biology, or medical laboratory science or technology in any combination.
- Have earned an associate degree in laboratory science or medical laboratory technology from an accredited institution.
- Have education and training equivalency to requirements specified at § 493.1489(b)(2)(i). Routes under this pathway include:
  - At least 60 semester hours, or equivalent, from an accredited institution that, at a minimum includes 24 semester hours of medical laboratory technology courses and have laboratory training that includes completion of a clinical laboratory training program approved or accredited by the Accrediting Bureau of Health Education Schools (ABHES) or the Commission

on Accreditation of Allied Health Education Programs (CAAHEP) (this training may be included in the required 60 semester hours).

- At least 60 semester hours, or equivalent, from an accredited institution that, at a minimum includes 24 semester hours of medical laboratory technology courses and have laboratory training that includes at least 3 months documented laboratory training in each specialty in which the individual performs high complexity testing.
- At least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, includes 24 semester hours of science courses that include: (i) six (6) semester hours of chemistry; (ii) six (6) semester hours of biology; and (iii) twelve (12) semester hours of chemistry, biology, or medical laboratory technology in any combination and have laboratory training that includes completion of a clinical laboratory training program approved or accredited by the Accrediting Bureau of Health Education Schools (ABHES) or the Commission on Accreditation of Allied Health Education Programs (CAAHEP) (this training may be included in the required 60 semester hours).
- At least 60 semester hours, or equivalent, from an accredited institution that, at a minimum, includes 24 semester hours of science courses that include: (i) six (6) semester hours of chemistry; (ii) six (6) semester hours of biology; and (iii) twelve (12) semester hours of chemistry, biology, or medical laboratory technology in any combination and have laboratory training that includes at least 3 months documented laboratory training in each specialty in which the individual performs high complexity testing.

- Successful completion of an official U.S. military medical laboratory procedures training course of at least 50 weeks duration and having held the military enlisted occupational specialty of Medical Laboratory Specialist (Laboratory Technician).
- Be qualified and serving as testing personnel of high complexity testing in a CLIA-certified laboratory as of December 28, 2024, and have done so continuously since December 28, 2024.

Appendix C

CLIAC Next Generation Sequencing (NGS) Workgroup Charge, Topics, and Discussion Questions

BACKGROUND

The Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations include federal standards applicable to all U.S. facilities or sites that test human specimens for health assessment or to diagnose, prevent, or treat disease. The CLIA regulations were finalized in 1992 and updated in 2003, with only limited updates since then.

As the types of test methods that use technologies such as Next Generation Sequencing (NGS) increase and with their broader uptake by laboratories, having a quality framework with qualified personnel in place is especially important. There are challenges when attempting to apply the almost 30-year-old CLIA regulations to these emerging technologies due to the novelty and complexity of the technology, new paradigms for data analysis, test result interpretation, and the bioinformatics portion of the test process.

The Centers for Disease Control and Prevention (CDC) obtained public comment through a Request for Information (RFI), Docket CDC 2020-0051, to gather feedback about the current state, challenges, and practices relevant to personnel performing bioinformatics activities in clinical and public health laboratories; storage and retention of NGS data files; and maintenance of sequence analysis software. The comment period closed in September 2020 with 16 responses from a diverse set of respondents that included reference laboratories, public health laboratories, academic clinical laboratories, professional societies, industrial partners, and private citizens. The NGS RFI summary report was presented during the November 2021 Clinical Laboratory Improvement Advisory Committee (CLIAC) meeting during the *NGS in Clinical and Public Health Laboratories* session. In addition to the summary report, a public health laboratory's experience with NGS validation and reporting was presented. The Committee deliberated, voted, and approved the following recommendation on the topic of NGS in Clinical and Public Health Laboratories:

CLIAC recommends that CDC, CMS, and FDA convene a workgroup to define the scope of practice and the requisite CLIA qualifications for personnel performing bioinformatics data analysis and interpretation to produce test results that inform clinical decision-making.

Workgroup topics and needed input:
Provide recommendations and cross-reference existing guidelines regarding education, training, experience, and competencies for various bioinformatics levels, for example:

- An MS or PhD level individual who provides analytic leadership, tool selection, and database oversight.
- A bioinformatics technician that, for example, ensures data files are appropriately formatted for analysis, to run the analysis, and to check for the adequacy of the run.
- The skill sets required for the Laboratory Director (MD/DO or PhD) who carries overall responsibility for the clinical laboratory.

Seek input from institutions of higher learning (universities) to develop, in concert with clinical laboratories, a curriculum and training for each level.

Engage certifying bodies (e.g., The American Board of Pathology and the American Society for Clinical Laboratory Science Board of Certification) in developing certification or other credentialing opportunities for clinical bioinformaticians who will work in CLIA laboratories.

The Next Generation Sequencing Workgroup is being established to provide input to CLIAC for deliberation on how CLIA might specifically be updated, considering the CDC NGS request for an information summary report, the April 2019 reports by the Personnel Regulations, Non-Traditional Workflow Models, and NGS workgroups, and the November 2021 CLIAC recommendation on personnel performing bioinformatics data analysis and interpretation. The focus of the workgroup is to define the scope of practice and the requisite CLIA qualifications for personnel performing NGS bioinformatics data analysis and interpretation to produce test results that inform clinical decision-making.

CHARGE

The workgroup is charged with providing advice to CLIAC for consideration in making recommendations to the Department of Health and Human Services (HHS) on education, training, experience, and competencies that should be required by CLIA to qualify personnel performing next generation sequencing bioinformatics data analysis and interpretation.

WORKGROUP DISCUSSION TOPICS

1. **Harmonization of definitions –** Creating or defining the fields/terms that will be used throughout workgroup discussions. Examples include:
    - Health/Laboratory Informatics
    - Bioinformatics
    - Clinical Informatics
    - Translational Informatics
    - Informatician
    - Bioinformatician

2. **What are the current regulatory requirements and guidelines related to the role of bioinformatics in clinical and public health laboratories performing NGS?**

3. **What is the current practice of bioinformatics in clinical and public health laboratories performing NGS?**

4. **Workgroup discussion education, training, experience, and competencies for various bioinformatics levels, including:**
    - An MS or PhD level individual who provides analytic leadership, tool selection, and database oversight.
    - A bioinformatics technician who, for example, ensures data files are appropriately formatted for analysis, runs the analysis, and checks for the adequacy of the run.
    - The skill sets required for the Laboratory Director (MD/DO or PhD) who carries overall responsibility for the clinical laboratory.

5. **Do the current CLIA regulations apply to the personnel discussed?**

DELIVERABLE

The output of the workgroup will be a summary report or periodic reports to CLIAC based on information gathered during teleconferences and potential face-to-face meetings and discussions. The reports will specifically address the priority topic areas and related questions. The workgroup Chair will present the reports at future CLIAC meetings for their deliberation and potential recommendations to HHS on the education, training, experience, and competencies that should be required by CLIA to qualify personnel performing next generation sequencing bioinformatics data analysis and interpretation. The report may

Appendix D

CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE (CLIAC)
NEXT GENERATION SEQUENCING (NGS) WORKGROUP ROSTER

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CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

Cybersecurity Requirements in Clinical Laboratories

November 7, 2024

Disclaimer

- This presentation was prepared for informational purposes and is not intended to grant rights or impose obligations. Every reasonable effort has been made to assure the accuracy of the information within these pages.

- This publication is a general summary that explains certain aspects of the Clinical Laboratory Improvement Amendments (CLIA) Program, but is not a legal document. The official CLIA Program provisions are contained in the relevant laws, regulations, and rulings. Links to the source documents have been provided within the document for your reference.

- The Centers for Medicare & Medicaid Services (CMS) employees, agents, and staff make no representation, warranty, or guarantee that this compilation of CLIA information is error-free and will bear no responsibility or liability for the results or consequences of the use of this guide.

Cybersecurity Requirements in Clinical Laboratories

Scope of the issue:[1]

- Ransomware attacks accounted for 70% of the successful cyberattacks on healthcare organizations
- 1,613 global healthcare organizations suffered an attack in the first 3 quarters of 2023
- Cyberattacks cost an average on $11 million per breach

State of the Industry: [2]

- More than one in four ransomware attacks affects patient care
- Approximately half of the healthcare organizations attacked said patient data was compromised
- More than one third of healthcare companies report not having a cybersecurity response plan

1 https://www.healthcarefinancenews.com/news/healthcare-cyberattacks-are-costing-average-11-million-breach
2 https://www.healthcaredive.com/news/healthcare-ransomware-cyberattack-impacts-patient-care-software-advice/716971/

Cybersecurity Requirements in Clinical Laboratories

Current CLIA cybersecurity regulatory requirements:

42 CFR 493.1251(b)(14)

The procedure manual must include the following when applicable to the test procedure:

- Description of the course of action to take if a test system becomes inoperable
  - Accompanying Interpretive Guidance: "*Laboratory information systems (LIS) procedures must be available to operators. Instructions should identify the individual(s), either by name or position, to notify if the LIS goes down or if a system error occurs.*"

Cybersecurity Requirements in Clinical Laboratories

Current CLIA cybersecurity regulatory requirements:

42 CFR 493.1291 Standard: Test report. The laboratory must have an adequate manual or electronic system(s) in place to ensure test results and other patient-specific data are accurately and reliably sent from the point of data entry (whether interfaced or entered manually) to final report destination, in a timely manner…

- Accompanying Interpretive Guidance: “If the laboratory uses a LIS or facsimile, what security measures have been instituted to ensure that transmitted reports go directly from the device sending reports to the authorized person, their personal representative (if applicable), and others who are identified as responsible for using the test results on the requisition? .”

Cybersecurity Requirements in Clinical Laboratories

Current CLIA cybersecurity regulatory requirements:
42 CFR 493.1254(a)(1) *Maintenance as defined by the manufacturer and with at least the frequency specified by the manufacturer.*

- The Interpretive Guidelines define "as defined by the manufacturer" to include each piece of equipment/instrument it uses, including those that are peripherally involved in patient testing. The guidance also explicitly states: *The laboratory must perform and document maintenance as specified by the manufacturer for the LIS computer and devices such as monitors, printers and modems. All devices must be maintained to ensure accurate, clear, and interference-free transmission.*
- The Interpretive Guidance offers specific probes to surveyors to help assess LIS functionality and cybersecurity: *Are LIS system components (e.g., server, hard drives, disk packs) maintained according to the manufacturer's instructions? When downtime is required to perform maintenance on LIS equipment, how are LIS users notified?*

Cybersecurity Requirements in Clinical Laboratories

- Recommendations from the NCC (National Computing Centre) Group as reflected in the January 16, 2024, edition of the Dark Report:
  - Employ multifactor authentication on all external facing internet connections
  - Segregate legacy operating systems from the network
  - Back up files in multiple offline locations
  - Create patches to address vulnerabilities frequently
  - Train staff is awareness of security threats
  - Draft and rehearse incident management plans

Cybersecurity Requirements in Clinical Laboratories

The questions for CLIAC on this topic:

Would CLIAC recommend stronger regulatory requirements related to cybersecurity protocols for the laboratory setting?

- What is the real-world risk of maintaining the status quo?
  - Weighing the likelihood of a cyberattack on a given laboratory
  - Assessing the current existing incentives to preventing an attack
- What is the cost of regulations that require the steps on the previous slide?
- What are the benefits of such regulations?
- How much time would a laboratory need to make such changes?

- Any alternative recommendations from CLIAC (Study group, RFI, etc.)

Cybersecurity Considerations for Clinical Laboratories

David McClintock, MD
Chair, Division of Computational Pathology & AI
Department of Laboratory Medicine and Pathology
Mayo Clinic

Disclosures

In the past 12 months, I have not had any significant financial interest or other relationship with the manufacturers of the products or providers of the services that will be discussed in my presentation.

Any vendors or manufacturers shown are for presentation purposes only and are not an endorsement on my part.

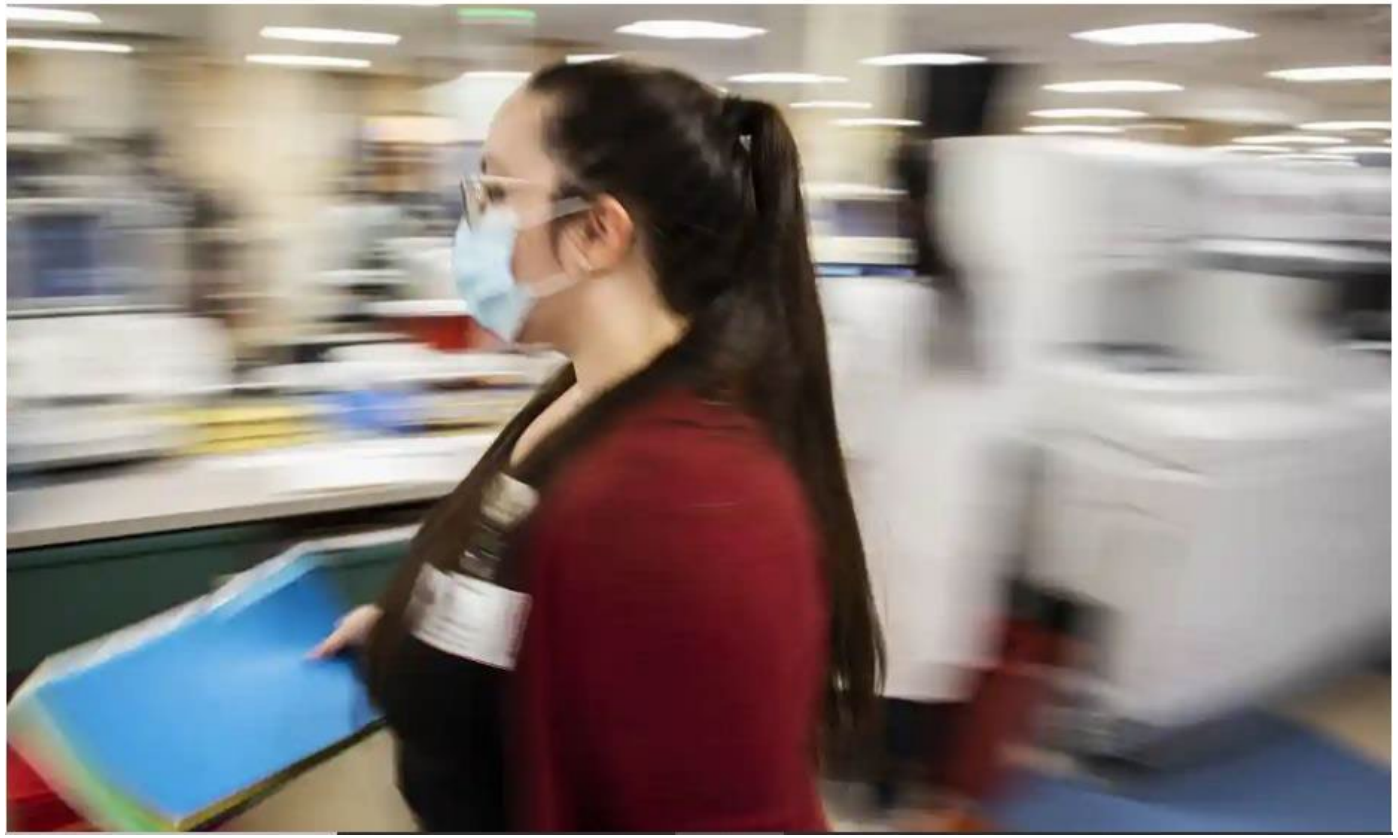
There is no way I can cover everything necessary on this topic in 20 minutes.

Cybersecurity is more prominent than ever!

Article from:
https://www.theguardian.com/technology/2022/jul/14/ransomware-attacks-cybersecurity-targeting-us-hospitals?via=indexdotco

‘Lives are at stake’: hacking of US hospitals highlights deadly risk of ransomware

The number of ransomware attacks on US healthcare organizations increased 94% from 2021 to 2022, according to one report



Article from: https://www.theguardian.com/technology/2022/jul/14/ransomware-attacks-cybersecurity-targeting-us-

Hackers are even hitting CHILDREN'S HOSPITALS!!

Article from: https://www.nbcnews.com/tech/security/lurie-childrens-hospital-chicago-cyber-attack-down-help-rcna137446

SECURITY

Parents struggle to get care after cyberattack on Chicago children's hospital

Hospital systems have been affected for more than a week.

Lurie Children's Hospital in Chicago. Alamy file

Feb. 8, 2024, 11:00 AM CST / Updated Feb. 8, 2024, 4:40 PM CST

By Kevin Collier

Chicago's biggest children's hospital, Ann & Robert H. Lurie Children's, has entered its second week of reduced service as it tries to recover from a cyberattack.

Most of the hospital's internet-connected equipment, including phones, email access and electronic health records, have been offline since the start of the incident, the hospital has said, making it significantly more difficult for parents to stay in touch with their doctors. Many appointments and surgeries are still being honored, the hospital said Monday.

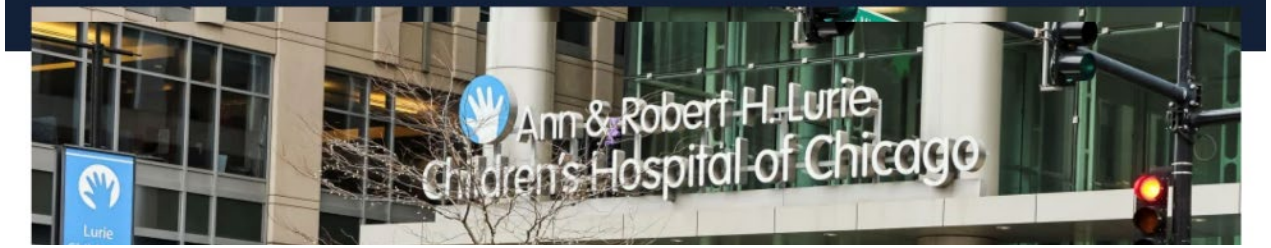
Hackers are HOSPITALS!!

NBC NEWS POLITICS U.S. NEWS WORLD BUSINESS SPORTS WATCH LIVE

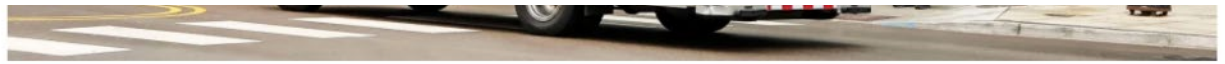
SECURITY

Parents struggle to get care after cyberattack on Chicago children's hospital

Hospital systems have been affected for more than a week.



"There is a special place in hell for a person who attacks a children's hospital and disrupts medical care for thousands of innocent children," said Deborah Land, whose teenage daughter is a patient at the hospital.



Lurie Children's Hospital in Chicago. Alamy file

Feb. 8, 2024, 11:00 AM CST / Updated Feb. 8, 2024, 4:40 PM CST

By Kevin Collier

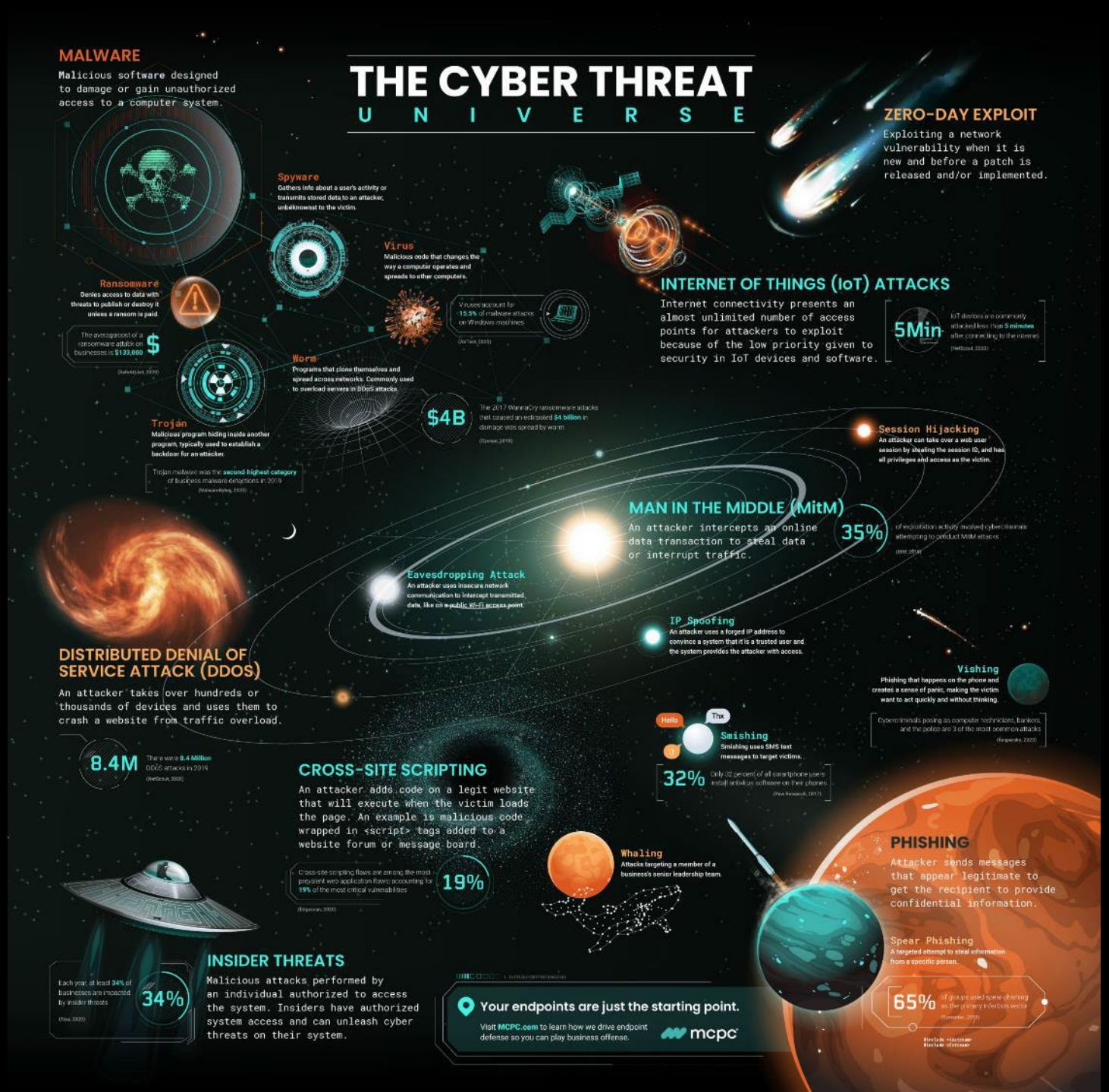
Chicago's biggest children's hospital, Ann & Robert H. Lurie Children's, has entered its second week of reduced service as it tries to recover from a cyberattack.

Most of the hospital's internet-connected equipment, including phones, email access and electronic health records, have been offline since the start of the incident, the hospital has said, making it significantly more difficult for parents to stay in touch with their doctors. Many appointments and surgeries are still being honored, the hospital said Monday.

Article from: https://www.nbcnews.com/tech/security/lurie-childrens-hospital-chicago-cyber-attack-down-help-rcna137446

Cyberthreats

Infographic from:
https://www.mcpc.com/insights/infographics/the-cyber-threat-universe/



Top Ten Cybersecurity Threats in 2024

1 Social Engineering

Any network is hackable if an employee can be duped into sharing access.

2 Third-Party Exposure

Vendors, clients, and app integrations with poor security can provide access to an otherwise well-protected network.

3 Configuration Mistakes

Even the most cutting-edge security software only works if it's installed correctly.

4 Poor Cyber Hygiene

Employee training is essential to ensure those with network access maintain safe cyber practices.

5 Cloud Vulnerabilities

Online data storage and transfer provides increased opportunities for a potential hack.

6 Ransomware

Hackers can capture sensitive data or take down networks and demand payment for restored access.

7 Mobile Device Vulnerabilities

Devices that connect to multiple networks are exposed to more potential security threats.

8 Internet of Things

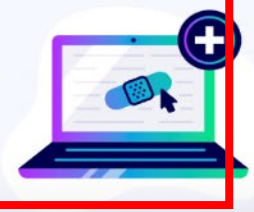
Smart technology users may not realize that any IoT device can be hacked to obtain network access.

9 Poor Data Management

When massive amounts of unnecessary data are kept, it's easier to lose and expose essential information.

10 Inadequate Post-Attack Procedures

Security patches must be as strong as the rest of your cybersecurity protections.



Source: https://www.embroker.com/blog/top cybersecurity threats/

Social Engineering

- Easier to trick a human than exploit a technical vulnerability in a system
  - Preys on human nature and emotional responses
  - ~85% of breaches involve human interaction
    - (2021 Verizon Data Breach Investigations Report)

- Social engineering techniques
  - 75% of data breaches start with an email!
    - Phishing, spear phishing, whaling
    - Vishing, smishing (phone calls, texting)

Verizon 2021 Data Breach Investigations Report, available at https://www.verizon.com/business/resources/reports/2021/2021-data-breach-investigations-report.pdf;

Spear Phishing

[3] [Liron Email] Greetings✅

From mailing2boxio00@gmail.com — Monday

To [redacted]

Are you still active on this email account?
I really require your help with something important.

Thanks
Liron Pantanowitz, MBBCh

Sent from AOL Desktop

From Liron Pantanowitz, MBBCh

To [redacted]

Glad to hear from you,

I need you to get an "Steam or Visa" gift card for
to get it for her today, but I can't do this now beca
lost his life to Coronavirus (covid19). Wondering
can handle this.

Await your soonest response.

Kind regards
Liron

From [redacted] — Monday

To mailing2boxio00@gmail.com

Hi Dr. Pantanowitz,

Hope you are doing well. I am, and this is probably the best place to reach me right now, [redacted]

How can I assist?

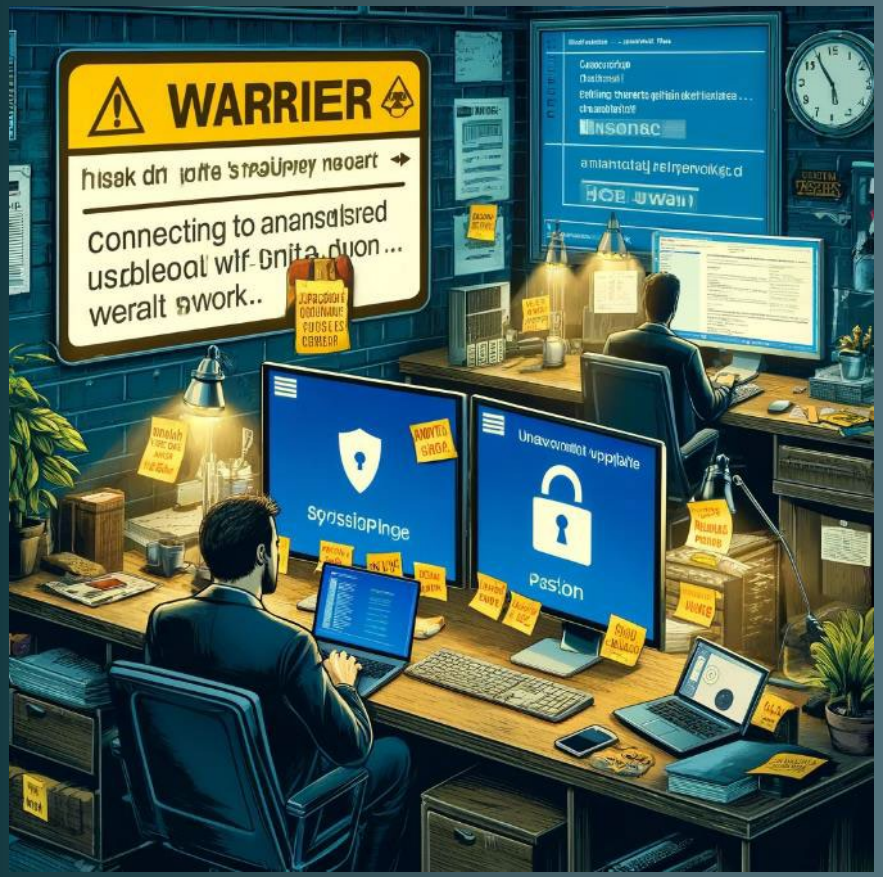
Regards,

Third Party Exposure

- Partners with privileged access to your systems
- GOAL:
  - Target 3rd party, less-protected systems with access to the hacker's primary target
- For clinical laboratories:
  - Middleware
  - Home grown systems based on open-source software
  - Legacy, must-have applications for your lab

Image: "Digital Illustration of Cyber Attack Targeting Strategy." Created by OpenAI's DALL-E, 04/26/2024.

Poor Cyber Hygiene

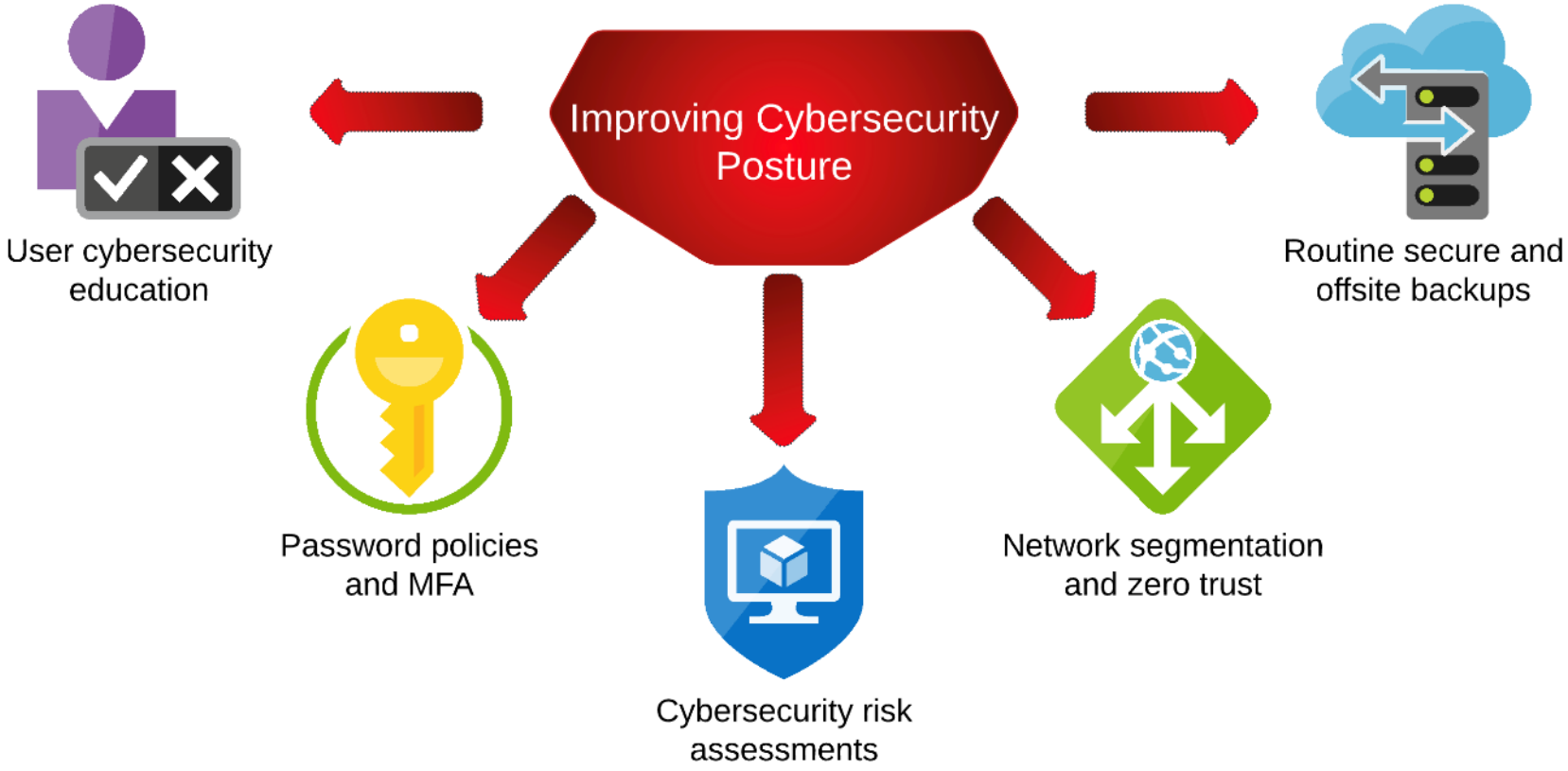


"Digital Illustration of Poor Cyber Hygiene in an Office." Created by OpenAI's DALL E, 04/28/2024

- **Cyber hygiene:**
  - Practices users take to maintain system health and improve cybersecurity
  - Relies on both the institution and its users to work together improve and maintain their overall cybersecurity posture
- **Cybersecurity posture**
  - Security status of an organization’s networks, information, and systems

Improving Cybersecurity Posture

- Cybersecurity posture is based on:
  - Information security resources (e.g., people, hardware, software, policies)
  - Capabilities in place to manage the enterprise's defense and to react as the situation changes



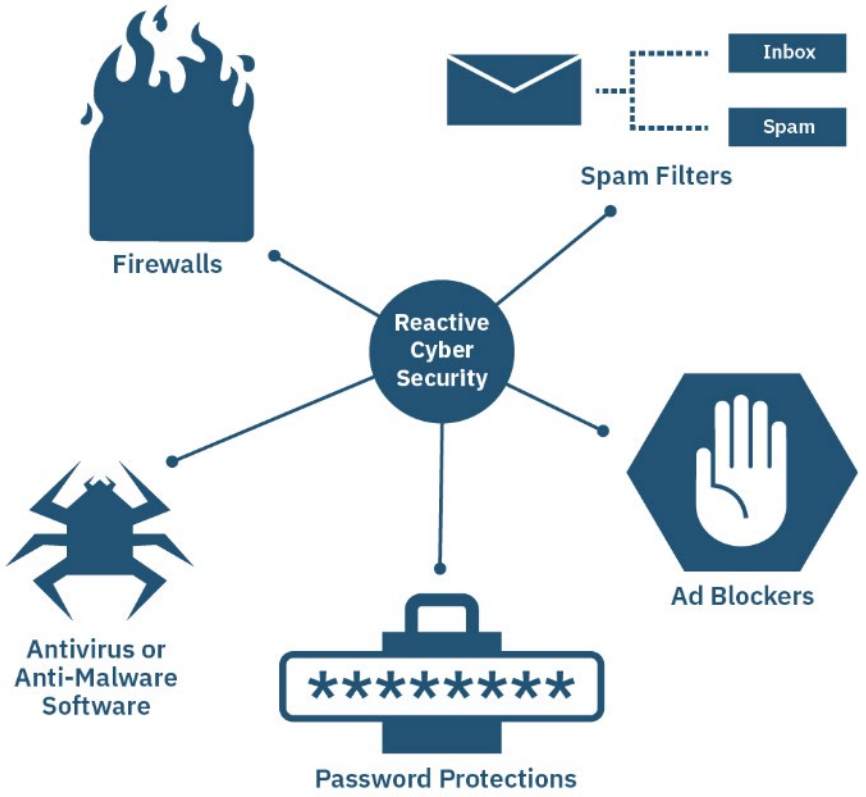
Cybersecurity Controls

Proactive cybersecurity controls

A proactive approach to cyber security locates and corrects your system's potential vulnerabilities before they can be exploited by criminals.

Reactive cybersecurity controls

A reactive approach to cyber security bulks up your defenses against common attacks and tracks down hackers inside your network.



Figures from: https://www.entrustsolutions.com/blog/proactive-vs-reactive-cyber-security/

User Cyber Hygiene Practices

- PC/device practices:
  - Core image machines / corporate standard builds
  - Limited privileges, approved applications/functions only, controlled use
  - Antivirus software, regular OS/software updates
  - Password change requirements, 2-factor authentication (2FA/MFA) use
  - Remote monitoring of PC use, network connections
  - Restrictions on who can use VPN and on which devices
- Mobile device management (MDM):
  - Laptops, tablets, phones, and other supported mobile devices
  - Examples: Microsoft InTune, VMWare Workspace One (Intelligent Hub)

Organizational Cyber Hygiene Practices

Network access

- NAC – network access control
- Network Segmentation
  - Clinical vs research vs guest networks
- Network traffic monitoring and control

Devices & storage

- Inventory / track all networked devices and storage media
- Require encryption and password protection
- Permission based access
- Establish retention policies, acceptable content policies

Applications

- Require SSO (single sign on) / Active Directory integration
- Disable local accounts whenever possible
- Perform regular risk assessments
- Integrate security reviews as part of every supply chain / procurement processes

Cloud Vulnerabilities

- Cloud vulnerabilities have reportedly increased 150% over the past five years
- More and more lab systems (digital pathology and AI systems especially) are using cloud-based systems
- Mitigation includes:
  - Moving to a zero-trust cybersecurity strategy
  - Becoming certified by HITRUST and other cybersecurity certifications
    - Certifiable framework providing global organizations a comprehensive, flexible, and efficient approach to regulatory/standards compliance and risk management; serves to demonstrate HIPAA Compliance

HITRUST®

Sources: 1) 2021 IBM Security X-Force Cloud Threat Landscape Report, available at https://www.ibm.com/downloads/cas/WMDZOWK6; 2) Verizon 2021 Data Breach Investigations Report, available at https://www.verizon.com/business/resources/reports/2021/2021-data-breach-investigations-report.pdf; 3) https://www.techment.com/top-5-cloud-vulnerabilities-to-consider-in-2022/

Cybersecurity Strategy: Castle and Moat

- Legacy strategy still used by some
- Focus on **strong network security perimeter → MOAT**
- Keep out malicious agents from **inner networks, systems, & data→ CASTLE**
- ***Once inside the castle, you have the keys to the kingdom!***
  - Great for internal users (easy access)
  - Bad for malicious agents (easy access!)
    - Cybercriminals
    - Internal bad actors/insider threats

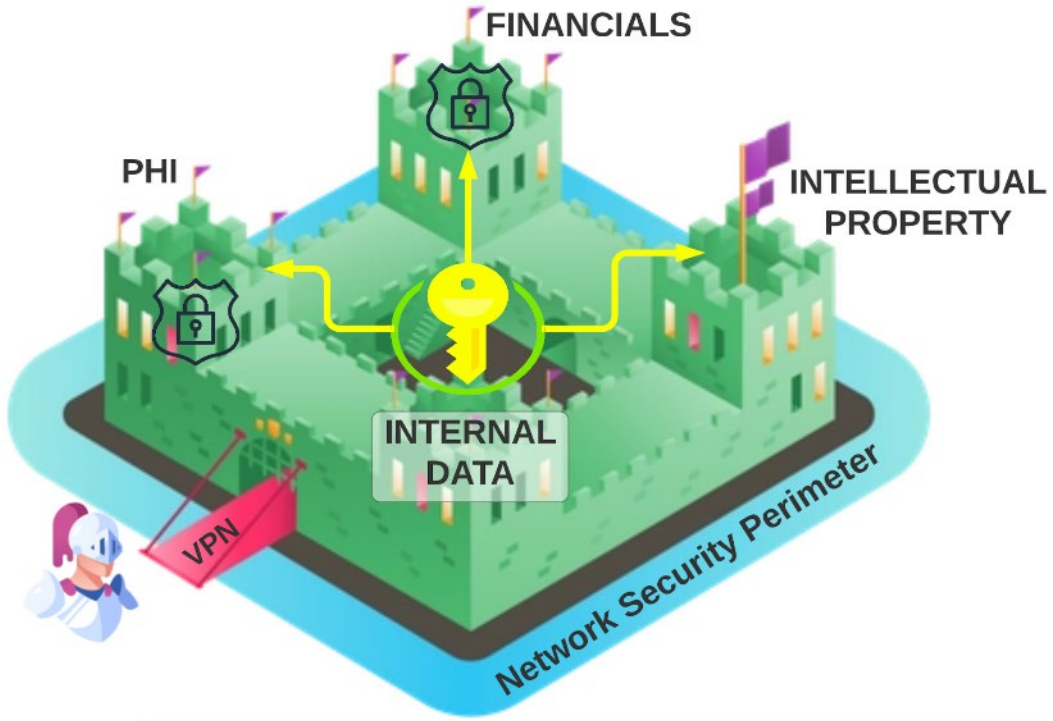


Figure from: Patel AU, Williams CL, Hart SN, Garcia CA, Durant TJS, Cornish TC, McClintock DS. Cybersecurity and Information Assurance for the Clinical Laboratory. J Appl Lab Med. 2023 Jan 4;8(1):145-161. doi: 10.1093/jalm/jfac119. PMID: 36610432.

Cybersecurity Strategy: Zero Trust

- Modern information security strategy
- **NO ONE CAN BE TRUSTED**
  - No central/single security perimeter/ moat, no keys to the kingdom
- ***Presumes risks are present both inside and outside the organization***
  - **ALL** incoming connections and source controls are verified throughout **ALL** layers of a network
  - Users/devices have to authenticate themselves when accessing practically every application within the organization

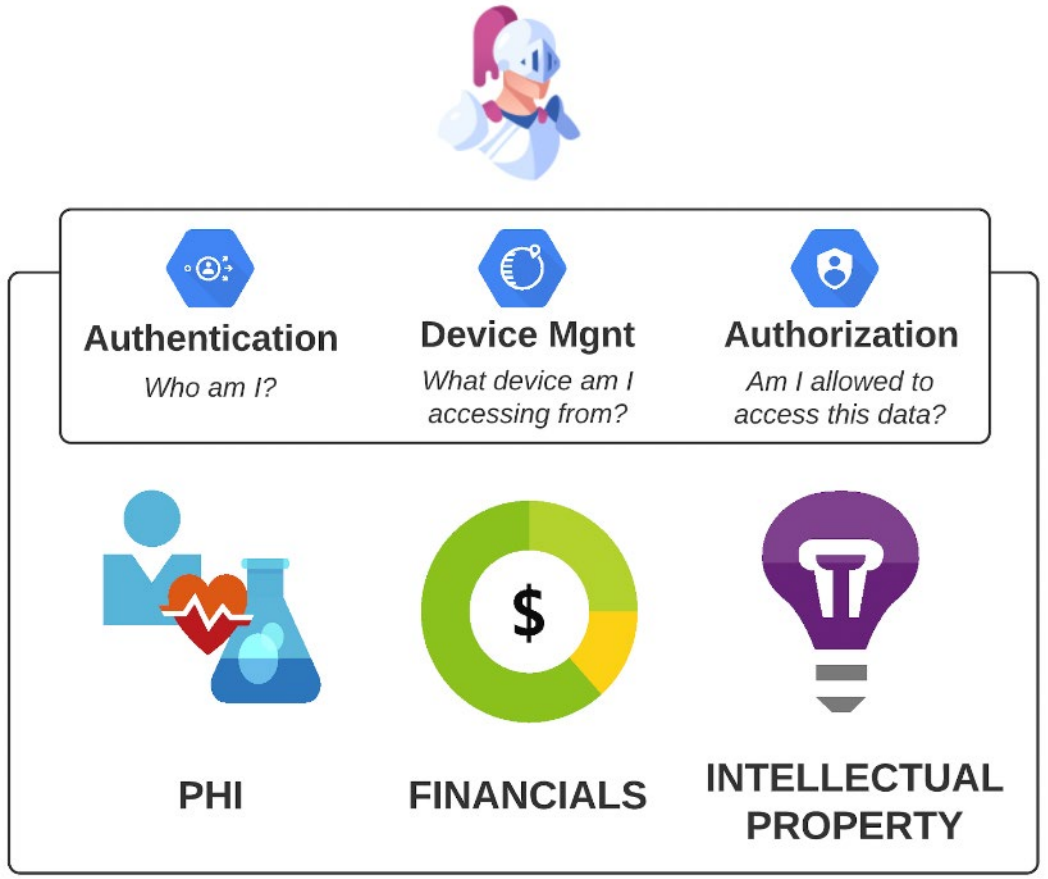


Figure from: Patel AU, Williams CL, Hart SN, Garcia CA, Durant TJS, Cornish TC, McClintock DS. Cybersecurity and Information Assurance for the Clinical Laboratory. J Appl Lab Med. 2023 Jan 4;8(1):145-161. doi: 10.1093/jalm/jfac119. PMID: 36610432.

Poor Data Management

- Data management today is more than just keeping your data organized
- What is the ”right” data to keep?
  - For some, all data is saved…but without organization and curation, think hoarders…
- Who has access to your data?
  - Who SHOULD be using your data and in what format?
  - Is your data easily accessible in a usable way?
- What changes in your pathology assets and data occur as more labs go digital
  - Think AP digitizing, less paper in lab medicine
- **With great data comes great responsibility**

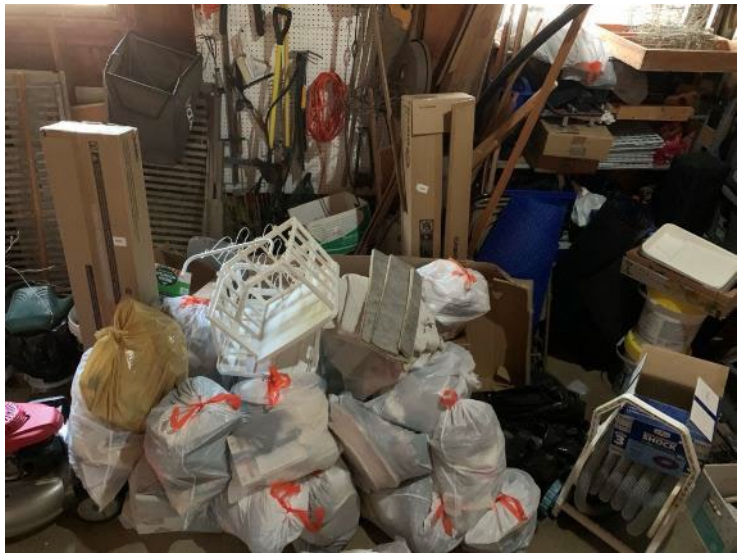


Image: My parents’ old garage…did my dad really need to keep everything??? Was it all important?

Data Management Changes for Digital Pathology

- Glass slides vs digital slides:
  - Glass slides
    - Limited distribution, only 1-2 patient identifiers if lost, person viewing slide has to know histopathology to learn more about the patient
  - Digital slides
    - Easily distributable, have metadata wrappers, contain varying degrees of patient identifiers and protected health information
  - Digital slides with annotations – same as digital slides, but with potentially much more actionable PHI
- Improper data management for DP can include:
  - Allowing improper access/use of clinical WSIs
  - Inadequate deidentification processes for WSIs
  - Slide labels embedded in the original WSIs for education/research

Infographic from: https://compliancy-group.com/18-hipaa-identifiers-for-phi/

Inadequate Post-Attack Procedures

- What happens in the event of a cyberattack? How does this differ from current lab downtimes?
  - Lab medicine and pathology practices require network connectivity now for almost everything!
  - When you have a ransomware attack, one of the first post-attack responses is to…SHUT DOWN THE NETWORK!
- For pathology → when going digital, you need ways to fall back to paper and glass!
  - Don’t throw out your microscope quite yet!

Strengthening Lab Preparations

- Cyberattacks can debilitate hospitals & labs for days to weeks
  - Labs need specific post-attack procedures that address how you react without any network connectivity
- Business continuity plans should include which lab systems are required when to help with bringing systems back online
- Third-party risk management reviews **(TPRM) ARE A MUST!**
  - Both internally developed and externally purchased solutions
  - ALL software applications, platforms, systems, and even laboratory hardware (equipment/devices), should be reviewed on a regular basis

Cyberattacks are real! And can decimate your lab…

Article from: https://www.captodayonline.com/weeks of lab turmoil follow cyberattack/

CAP TODAY

PATHOLOGY • LABORATORY MEDICINE • LABORATORY MANAGEMENT / APRIL 2021

Weeks of lab turmoil follow cyberattack

Anne Paxton

After he finished interviewing for a fellowship one morning last October at the University of Vermont Medical Center, pathology resident William O. Humphrey, MD, checked in to attend grand rounds virtually. Then the cyberattack struck.

First of two parts
Next month: cybersecurity

It began mysteriously, with people dropping one by one off the Zoom screen and emails arriving only intermittently. Internet service grew patchy and a hospital staffer unmuted and canceled grand rounds, saying, "We aren't really sure what's going on."

From there, a cascade of failures indicated serious trouble. "All of a sudden we're realizing we can't sign into our EMR. We can't get into our email either. My phone isn't working on the Wi-Fi. Something is wrong," recalls Dr. Humphrey, a member of the CAP Informatics Committee. That was the prelude to a siege in which fax machines and penmanship were unretired from obsolescence, paperlessness became a relic of the past, and words like "runners" and "bouncers" entered routine laboratory vocabulary.

External agents had maliciously invaded and at least partially disabled the system. "It was certainly something abrupt. And our impression was that it may have been related to email phishing," Dr. Humphrey says, though no official word to hospital staff has clarified how it occurred and who engineered it and why.

Such attacks have become a serious risk for any enterprise reliant on IT, which in this decade is nearly all enterprises. But cyber- —continued on 12

David Seiver

Dr. Andrew Goodwin (from left), Dr. Christina Wojewoda, and Dr. William Humphrey at the University of Vermont Medical Center, where a cyberattack last fall sent the lab into prolonged downtime and chaos. "A cyberattack shuts down much more than you anticipated," Dr. Goodwin says.

'Know your panel': Blood culture ID cautions

Amy Carpenter Aquino

The interpretive challenges of blood culture identification panels were the focus of an AMP2020 virtual presentation on false-positives and false-negatives and their sources and solutions.

The spotlight was on *Proteus*, but "it's not the sole organism we have to worry about," said Susan Butler-Wu, PhD, D(ABMM), SM(ASCP), director of the clinical microbiology laboratory, LAC+USC Medical Center, Los Angeles, and associate professor of clinical pathology, Keck School of Medicine of USC.

Her co-presenter, speaking on antimicrobial resistance targets, was Richard Davis, PhD, D(ABMM), MLS(ASCP)^{CM}, of Providence Healthcare. (See CAP TODAY, May 2021, for coverage.) Dr. Davis and Dr. Butler-

Cyberattacks have real consequences – would your lab survive without the internet?

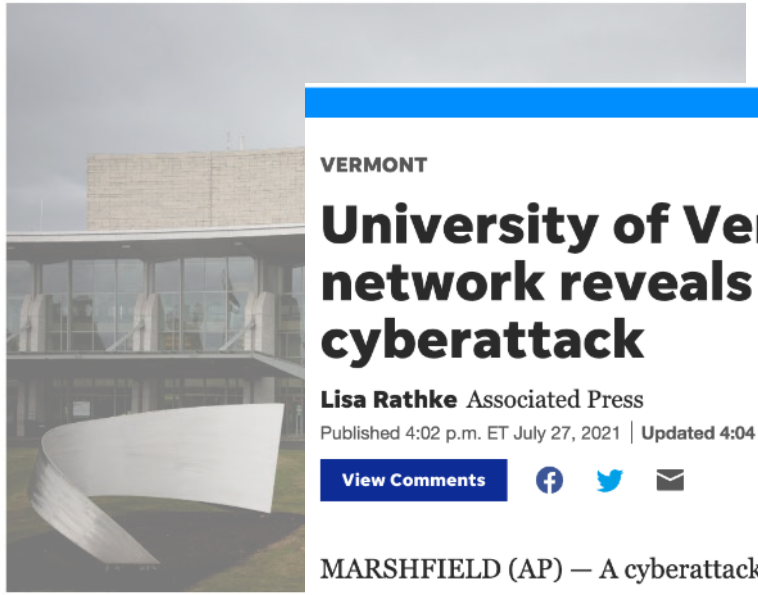
Articles from:

1. https://www.burlingtonfreepress.com/story/news/local/vermont/2021/07/27/uvmmc vermont health network hospital 2020 cyberattack cause malware phishing vermont hospital/5388399001/
2. https://www.usnews.com/news/best states/vermont/articles/2020 12 09/recovery cost of vermont hospital cyberattack could be 63m
3. https://www.nytimes.com/2020/11/26/us/hospital cyber attack.html

The New York Times

Patients of a Vermont Hospital Are Left 'in Dark' After a Cyberattack

A wave of damaging attacks on hospitals upended the lives of pa cancer and other ailments. "I have no idea what to do," one said.



The University of Vermont Medi in late October. Elizabeth Frantz f

By Ellen Barry and Nicole Perlrot

Published Nov. 26, 2020 Updated

At lunchtime on Oct. 28, University of Vermont M chemotherapy infusions. frightened, but the nurse a warm blanket, a seat w

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Vermont Hospital Cyberattack Cost Estimated at $1.5M a Day

University of Vermont Medical Center officials say a late October cyberattack is costing the hospital about $1.5 million a day.

By Associated Press | Dec. 9, 2020

tack on the computer systems osting the hospital about $1.5 its CEO said.

ns of the hospital system that ew York.

VERMONT

University of Vermont hospital network reveals cause of 2020 cyberattack

Lisa Rathke Associated Press

Published 4:02 p.m. ET July 27, 2021 | **Updated 4:04 p.m. ET July 27, 2021**

View Comments

MARSHFIELD (AP) — A cyberattack that crippled the computer systems of a hospital network affecting six hospitals in Vermont and New York last fall happened after an employee opened a personal email on a company laptop while on vacation, a University of Vermont Health Network official said Tuesday.

The email was from legitimate local business that had been hacked, Doug Gentile, network chief medical information officer told The Associated Press. The email contained an attachment that had the malware. When the employee returned from vacation and logged onto the UVM network through a virtual private network, the attackers were ready and launched the attack, he said.

"We have no evidence at all that UVM was specifically targeted. We just got caught up in a broad phishing attack," Gentile said Tuesday.

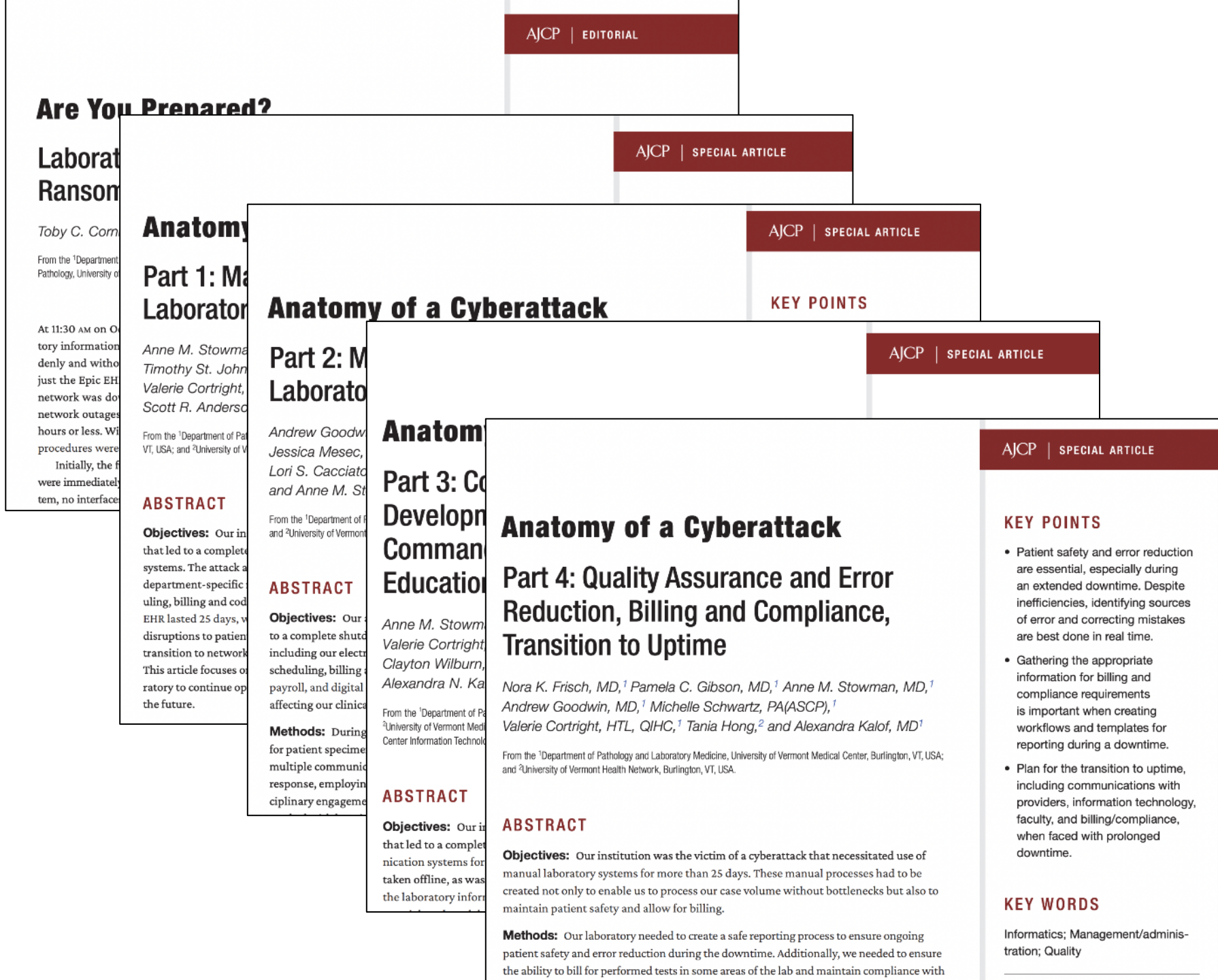
Series of five publications, reviews how to better prepare for a cyberattack – THIS IS ESSENTIAL READING!

INSIDE THE LAB

PODCAST EPISODE

S2Ep17: Anatomy of a Cyberattack

Inside the Lab



Review to help drive home concepts

Patel AU, Williams CL, Hart SN, Garcia CA, Durant TJS, Cornish TC, McClintock DS. Cybersecurity and Information Assurance for the Clinical Laboratory. J Appl Lab Med. 2023 Jan 4;8(1):145-161. doi: 10.1093/jalm/jfac119. PMID: 36610432.

Available at: https://academic.oup.com/jalm/article/8/1/145/6965173?login=false

REVIEW

Cybersecurity and Information Assurance for the Clinical Laboratory

Ankush U. Patel,[a,†] Christopher L. Williams,[b,†] Steven N. Hart ,[a] Christopher A. Garcia,[a] Thomas J.S. Durant,[c] Toby C. Cornish ,[d] and David S. McClintock [a,*]

Background: Network-connected medical devices have rapidly proliferated in the wake of recent global catalysts, leaving clinical laboratories and healthcare organizations vulnerable to malicious actors seeking to ransom sensitive healthcare information. As organizations become increasingly dependent on integrated systems and data-driven patient care operations, a sudden cyberattack and the associated downtime can have a devastating impact on patient care and the institution as a whole. Cybersecurity, information security, and information assurance principles are, therefore, vital for clinical laboratories to fully prepare for what has now become inevitable, future cyberattacks.

Content: This review aims to provide a basic understanding of cybersecurity, information security, and information assurance principles as they relate to healthcare and the clinical laboratories. Common cybersecurity risks and threats are defined in addition to current proactive and reactive cybersecurity controls. Information assurance strategies are reviewed, including traditional castle-and-moat and zero-trust security models. Finally, ways in which clinical laboratories can prepare for an eventual cyberattack with extended downtime are discussed.

Summary: The future of healthcare is intimately tied to technology, interoperability, and data to deliver the highest quality of patient care. Understanding cybersecurity and information assurance is just the first preparative step for clinical laboratories as they ensure the protection of patient data and the continuity of their operations.

Final Thoughts

- Many cybersecurity risks exist today!
- There is no 100% secure, or zero risk system
  - Cybersecurity should be equated to continuous QA/QM in the labs
- **RECOMMENDATION: Become part of the process**
  - Actively seek out your information security team(s)
  - Be a part of the information security process
- At some point, you will likely be part of a cyberattack and it will suck


QUESTIONS?

Proficiency Testing (PT) Program Content

Angelique Daubert

Division of Clinical Laboratory Improvement and Quality

November 07, 2024

Disclaimer

- This presentation was prepared for informational purposes and is not intended to grant rights or impose obligations. Every reasonable effort has been made to assure the accuracy of the information within these pages.

- This publication is a general summary that explains certain aspects of the Clinical Laboratory Improvement Amendments (CLIA) Program, but is not a legal document. The official CLIA Program provisions are contained in the relevant laws, regulations, and rulings. Links to the source documents have been provided within the document for your reference.

- The Centers for Medicare & Medicaid Services (CMS) employees, agents, and staff make no representation, warranty, or guarantee that this compilation of CLIA information is error-free and will bear no responsibility or liability for the results or consequences of the use of this guide.

PT Program Approval Process

- An organization, Federal, or State program seeking approval or reapproval for its program for the next calendar year must submit an application providing the required information by July 1 of the current year. (§ 493.901 Approval of proficiency testing programs.)
- CMS partners with CDC to approve PT programs annually.
  - In general, CMS focuses on evaluating the information about program administration and proposed content for the upcoming calendar year, while CDC focuses on analyzing the data from the PT program's previous year's offerings to ensure they met the regulatory guidelines.

PT Program Content Requirements

- The annual program must provide samples that cover the **full range of reactivity** from highly reactive to non-reactive. (Syphilis serology § 493.923(a) and general immunology § 493.927(a))

- The annual program must provide samples that cover the **clinically relevant range** of values that would be expected in patient specimens. (Routine chemistry § 493.931(a) and endocrinology § 493.933(a))

- The annual program must provide samples that cover the full range of values that could occur in patient specimens and that cover the **level of clinical significance** for the particular drug. (Toxicology § 493.937(a))

PT Program Content Requirements (cont.)

- The annual program must provide samples that cover the **full range of values** that would be expected in patient samples. (Hematology § 493.941(a))

- The annual program must provide samples that cover the **full range of interpretation** that would be expected in patient samples. (Immunohematology § 493.959(b))

Challenges for PT Programs

- Providing samples on the low-end of the range.
  - Examples: Alanine aminotransferase (ALT), Alkaline Phosphatase, Aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatine kinase, creatinine, Thyroid Stimulating Hormone (TSH), T3 uptake, protime, partial thromboplastin time, carbamazepine, valproic acid.
- Samples need to cover multiple instruments, methodologies, reagents, and analytes.

Division of Laboratory Systems

Proficiency Testing (PT) Program Evaluation: Selection and Use of Reference Ranges

Víctor R. De Jesús, PhD

Acting Director, Division of Laboratory Systems
Office of Laboratory Systems and Response
CDC Ex-officio, Clinical Laboratory Improvement Advisory Committee

Reference Ranges

- Reference ranges are used to determine if analyte challenges are provided across the relevant range of reactivity, values, interpretation, clinical significance, or clinical relevance

- For each analyte, the values from the total population of laboratories or the largest number of laboratories are recorded and compared to the reference range

CDC expects that of the 15 annual challenges, at least one is within 10% of the lowest or highest reference value to be considered compliant

Most reference ranges are from the Mayo Clinic Test Menu website (Home - Mayo Clinic Laboratories)

For the five analytes not found on the Mayo Clinic Test Menu website, other public access websites were searched

- The five analytes not found on the Mayo Clinic Test Menu:
  - Blood gases - medlineplus./gov/encyclopedia.html
  - Creatine Kinase MB - www.aruplab.com/testing
  - Lactate Dehydrogenase Isoenzymes - www.labcorp.com/test-menu/search
  - T3 Uptake - www.labcorp.com/test-menu/search
  - White blood cell differential

- White blood cell differential
  - No specific laboratory reference range used
  - Different sets of challenges are sent based on the instrument used
  - Analysis used values from the instrument operated by most laboratories
    - The average of each analyte from each PT program was calculated
    - Reference range was the span of the average values

Thank you!

Víctor R. De Jesús, PhD
vdejesus@cdc.gov

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Discussion Questions

Discussion questions for CLIAC on this topic:

- How should we determine the sample range for each analyte that a PT program should cover?
  - Clinically relevant range
  - Full range of reactivity
  - Level of clinical significance
  - Full range of values
- What are acceptable limitations to proficiency testing programs meeting these ranges?

MAYO CLINIC

PROFICIENCY TESTING

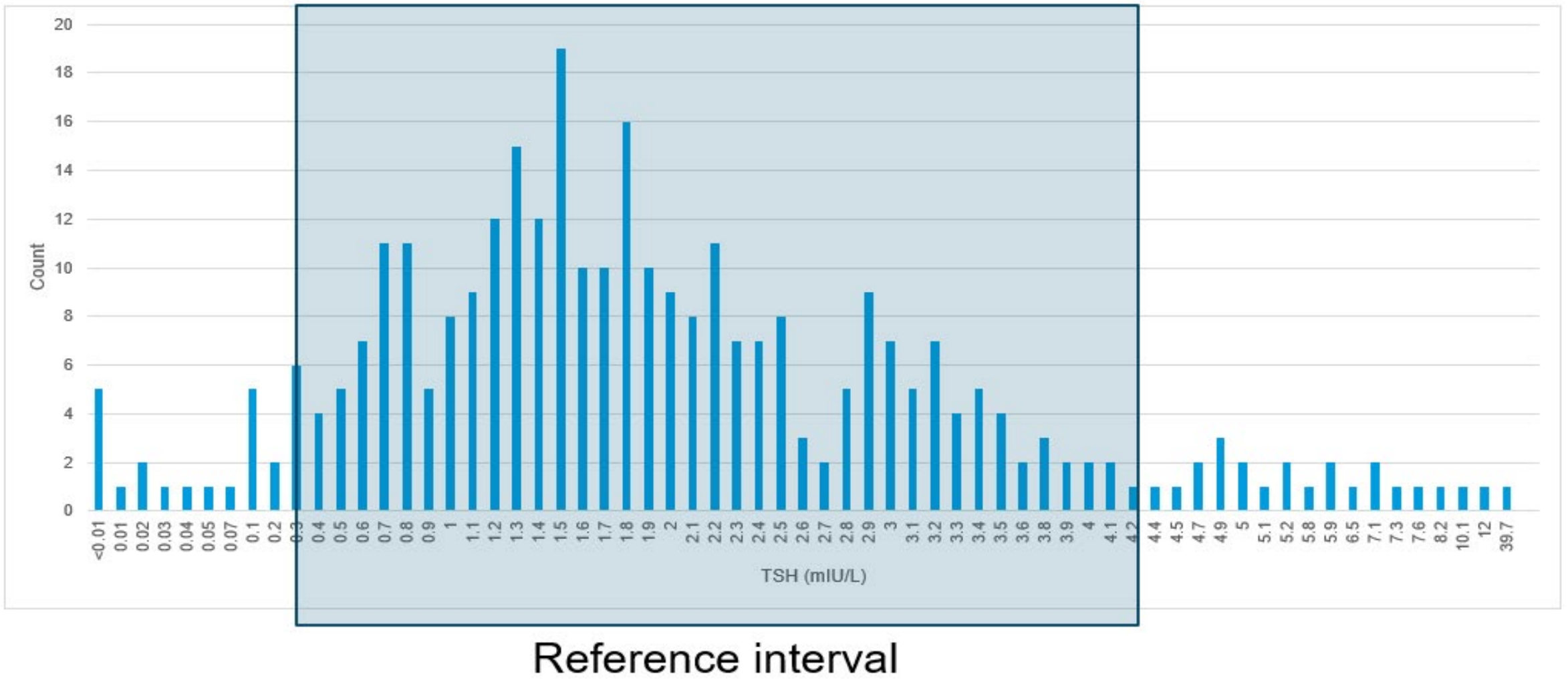
MEASURING THE CLINICALLY RELEVANT RANGE OF VALUES

Nikola A. Baumann, Ph.D.
Vice Chair of Quality,
Co-Director, Central Clinical Laboratory and Central Processing Laboratory
Director, Process Innovation through Automation (PITA) Laboratory,
Department of Laboratory Medicine and Pathology
Mayo Clinic, Rochester, MN

WHAT IS THE CLINICALLY RELEVANT RANGE OF VALUES FOR AN ASSAY?

Reference intervals	Interval of values observed in healthy subjects (central 95th %)

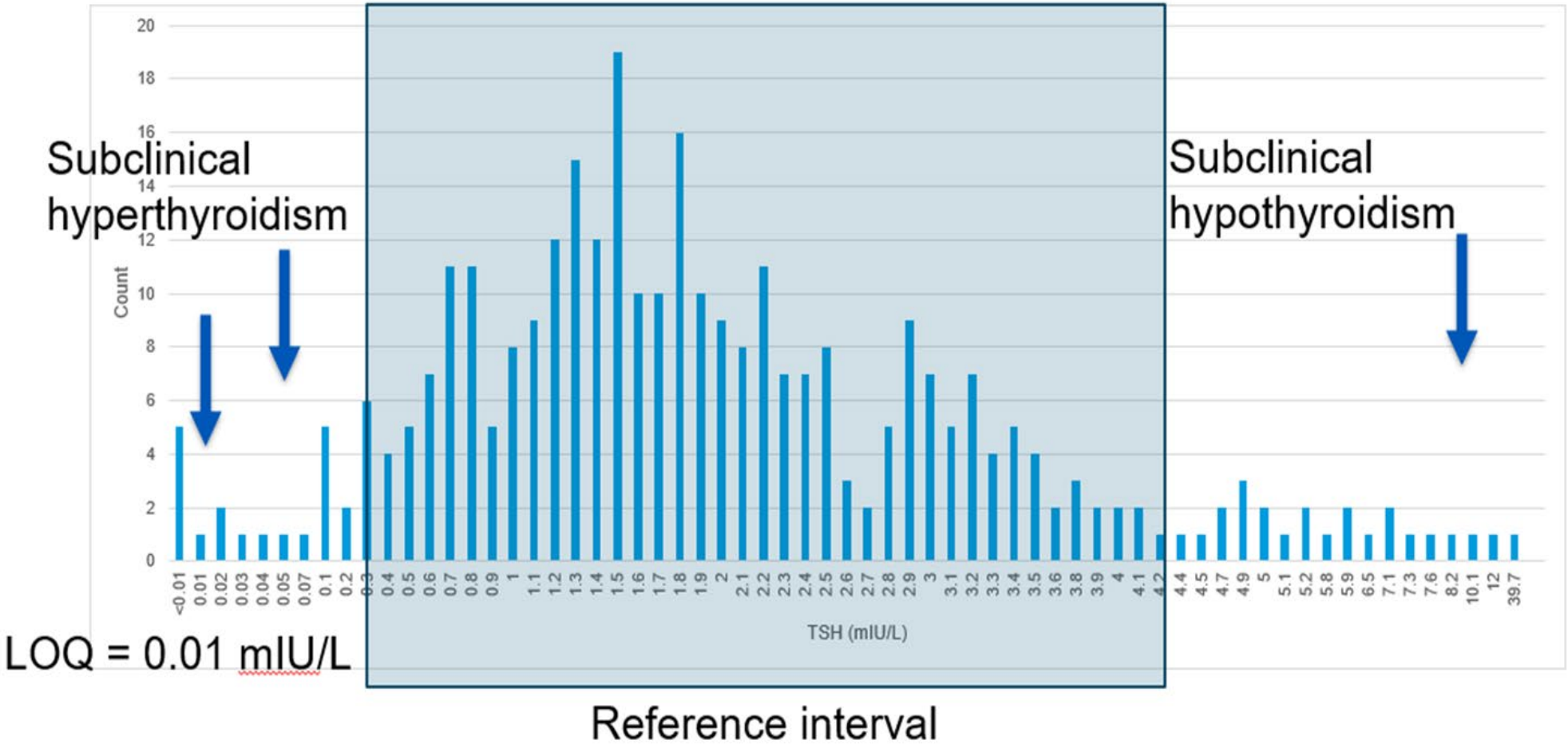
DISTRIBUTION OF THYROID STIMULATING HORMONE (TSH) RESULTS



WHAT IS THE CLINICALLY RELEVANT RANGE OF VALUES FOR AN ASSAY?

Reference intervals	Interval of values observed in healthy subjects (central 95th %)
Medical decision points	Pos/Neg Indicator of disease/risk Intervention

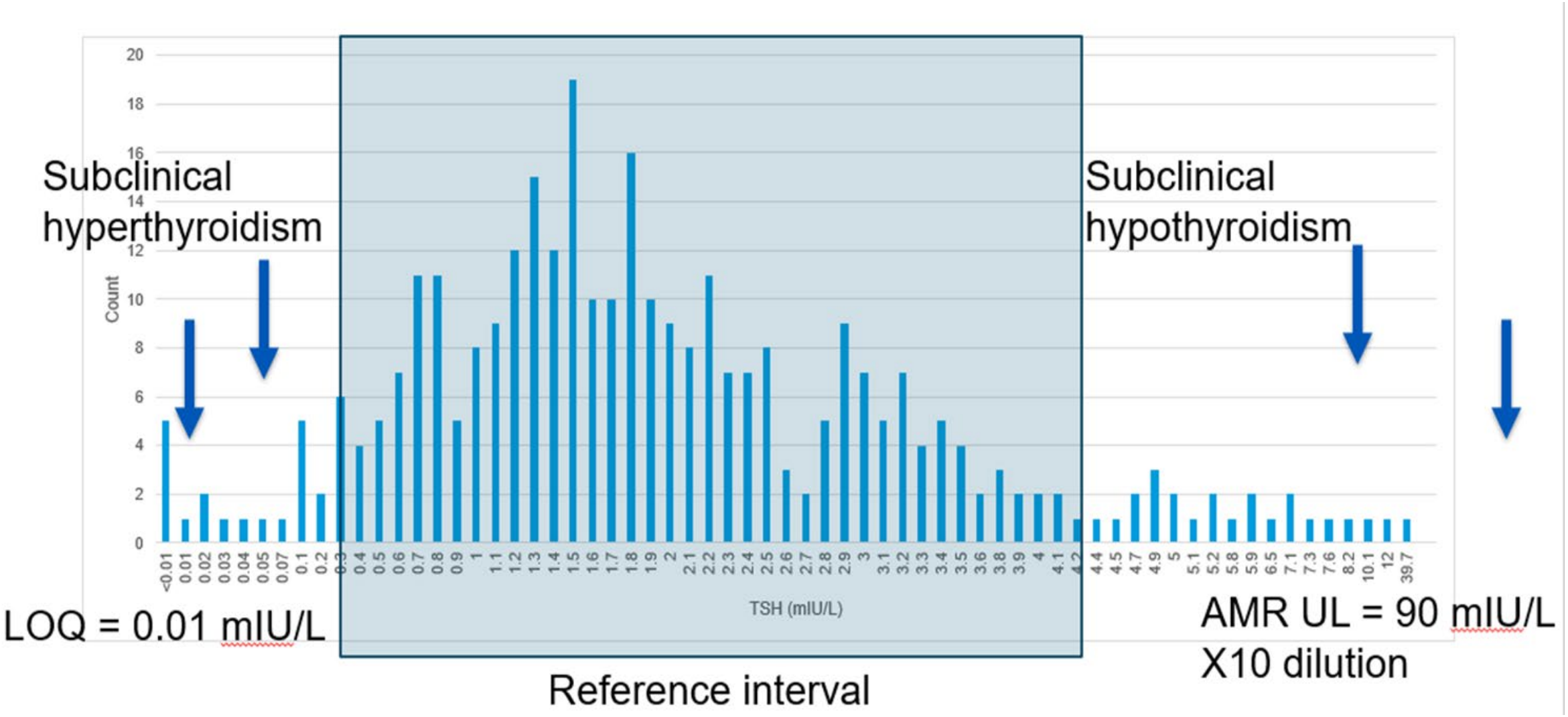
DISTRIBUTION OF THYROID STIMULATING HORMONE (TSH) RESULTS



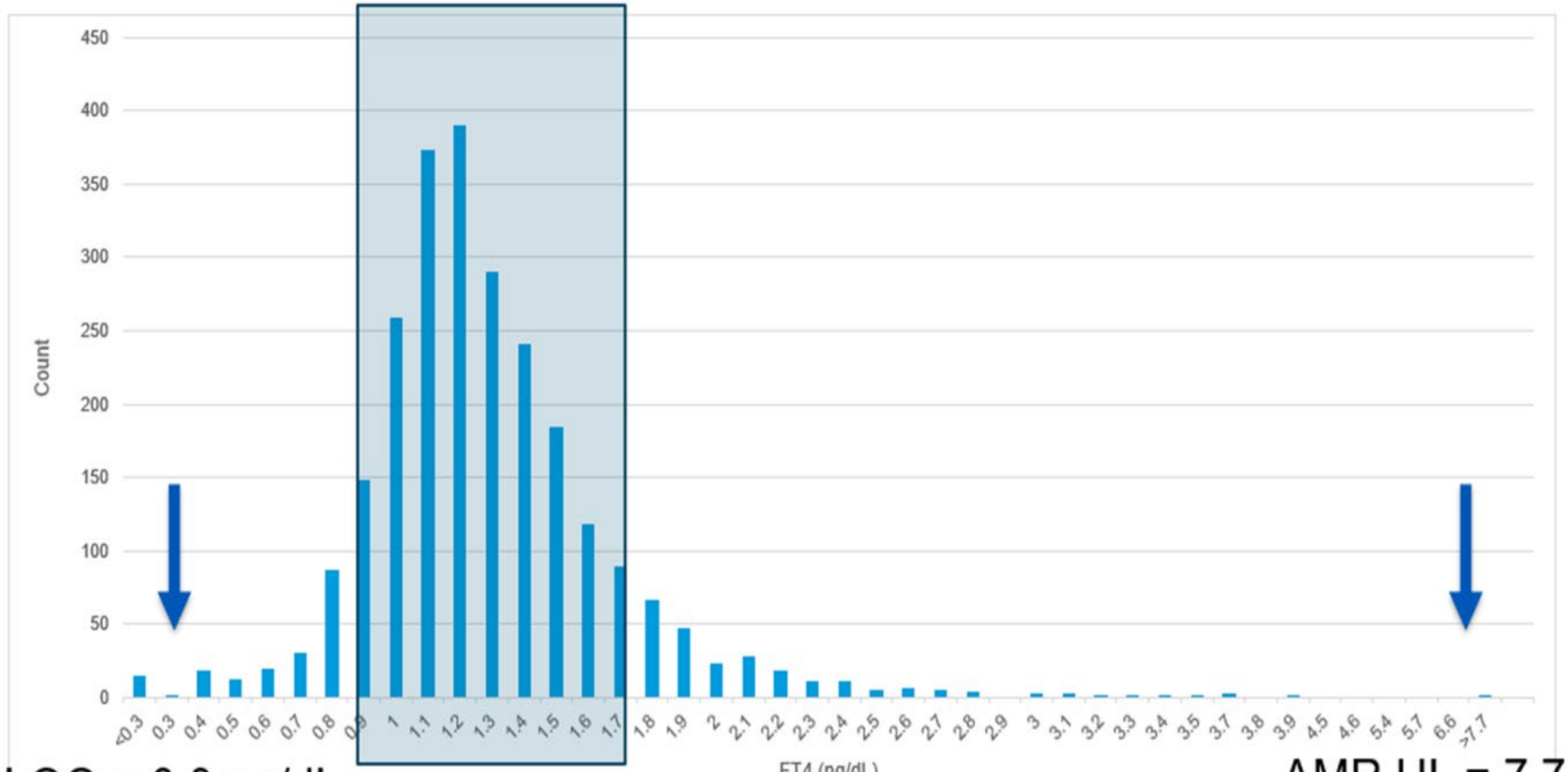
WHAT IS THE CLINICALLY RELEVANT RANGE OF VALUES FOR AN ASSAY?

Reference intervals	Interval of values observed in healthy subjects (central 95th %)
Medical decision points	Pos/Neg Indicator of disease/risk Intervention
Delta (change over time)	Reference change value Response to treatment

DISTRIBUTION OF THYROID STIMULATING HORMONE (TSH) RESULTS



DISTRIBUTION OF FREE THYROXINE (FT4) RESULTS



LOQ = 0.3 ng/dL

Reference Interval ~
Medical Decision Limit

AMR UL = 7.7 ng/dL
Critical value

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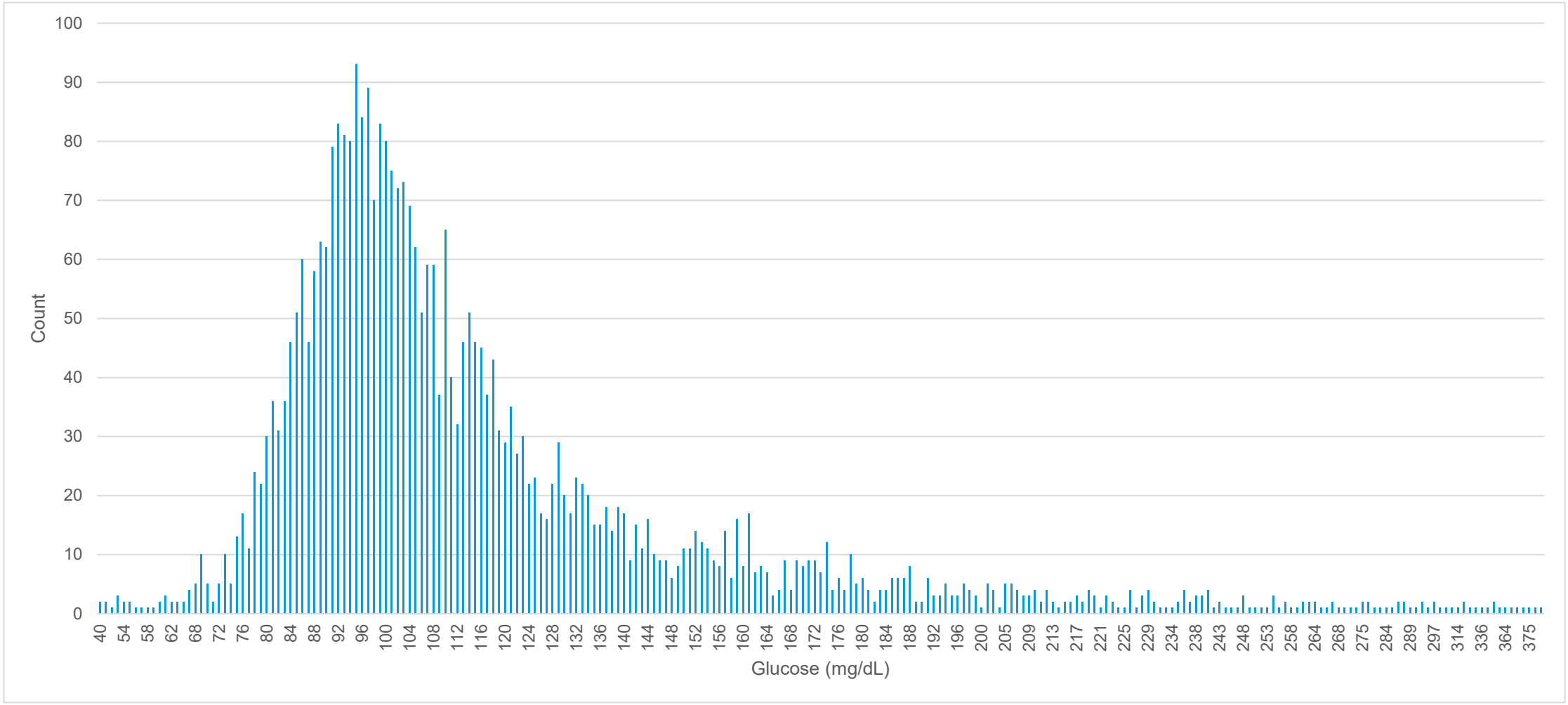
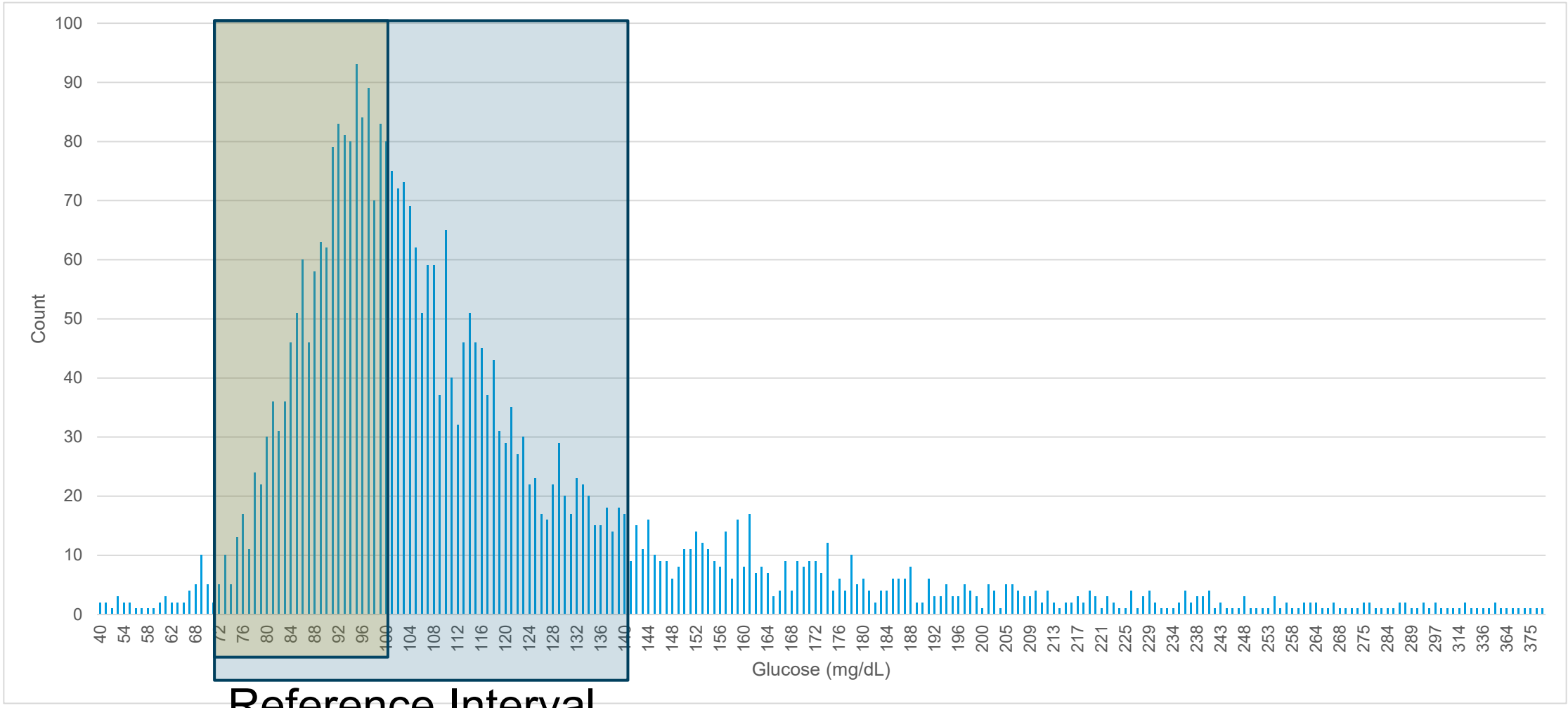
WHAT IS THE CLINICALLY IRRELEVANT RANGE OF VALUES FOR AN ASSAY?

Physiologically improbable results within the AMR

DISTRIBUTION OF SERUM GLUCOSE RESULTS

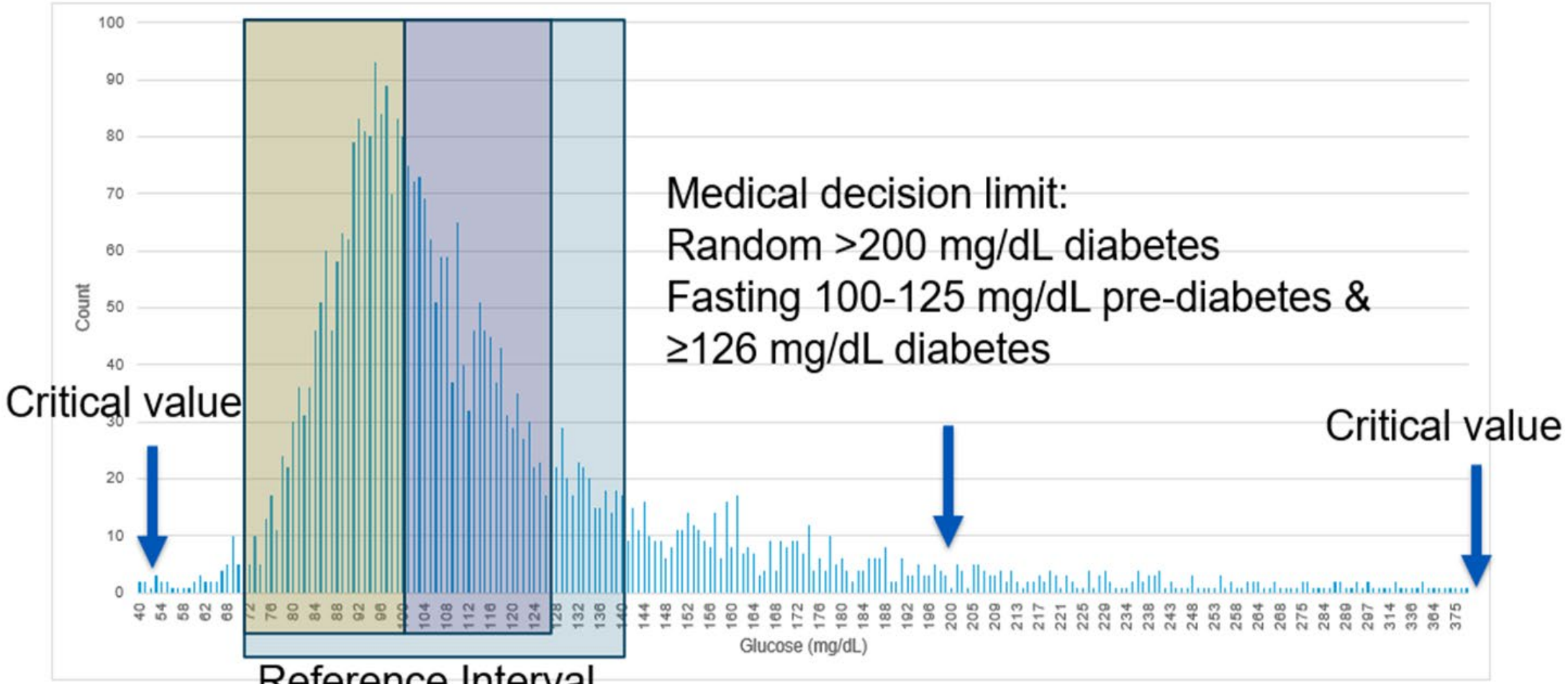


DISTRIBUTION OF SERUM GLUCOSE RESULTS

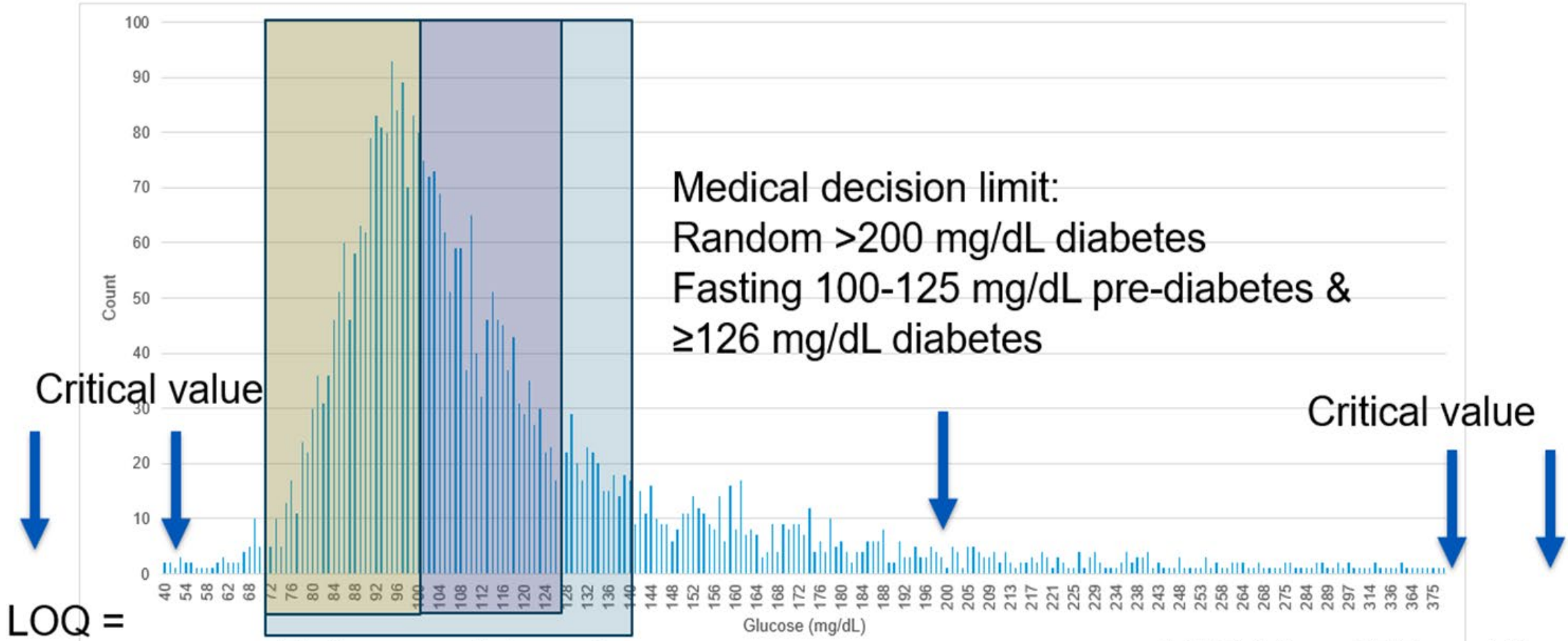


Reference Interval
Random 70-140 mg/dL
Fasting 70-100 mg/dL

DISTRIBUTION OF SERUM GLUCOSE RESULTS



DISTRIBUTION OF SERUM GLUCOSE RESULTS



WHAT IS THE CLINICALLY IRRELEVANT RANGE OF VALUES FOR AN ASSAY?

Physiologically improbable results within the AMR:

Example: glucose between 2 mg/dL – 30 mg/dL

Extremes of measurement ranges

WHAT IS THE CLINICALLY IRRELEVANT RANGE OF VALUES FOR AN ASSAY?

Physiologically improbable results within the AMR:

Example: glucose between 2 mg/dL – 30 mg/dL

Extremes of measurement ranges

Caveat: Labs are accountable for accuracy within the AMR (independent of clinical relevance)

ACCOUNTABILITY: ANALYTICAL PERFORMANCE CHARACTERISTICS

Precision	Accuracy	Analytical measurement range	Reportable range	Reference intervals
• Reproducibility	• Truth	• Linearity • Recovery	• Dilution • Concentration	• Method • Population

CLINICALLY RELEVANT RANGE OF VALUES

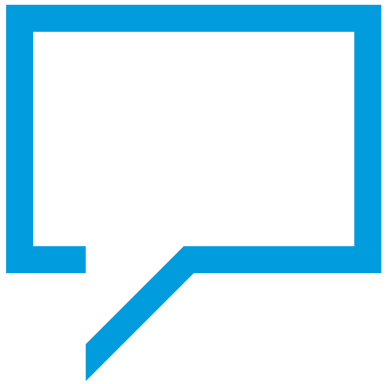
Data-driven approach

Determine clinically irrelevant range of values

Considerations

- Reference intervals
- Medical decision limits
- Change in values over time

QUESTIONS & ANSWERS



CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

Virtual Competency Assessments

November 7, 2024

Disclaimer

- This presentation was prepared for informational purposes and is not intended to grant rights or impose obligations. Every reasonable effort has been made to assure the accuracy of the information within these pages.

- This publication is a general summary that explains certain aspects of the Clinical Laboratory Improvement Amendments (CLIA) Program, but is not a legal document. The official CLIA Program provisions are contained in the relevant laws, regulations, and rulings. Links to the source documents have been provided within the document for your reference.

- The Centers for Medicare & Medicaid Services (CMS) employees, agents, and staff make no representation, warranty, or guarantee that this compilation of CLIA information is error-free and will bear no responsibility or liability for the results or consequences of the use of this guide.

Virtual Competency Assessments in Clinical Laboratories

Historical view of virtual competency assessments:

- 71% of state agencies polled were not in favor of virtual competency assessments (2022)
- 75% of CMS CLIA locations were not if favor of virtual competency assessments (2022)
- 50% of Accrediting Organizations were opposed/not opposed
- Support for opposition to the technology cites competency assessments as the single most frequently cited deficiency in CLIA surveys.

We are clearly a pretty change adverse group.

Competency Assessment Requirements in Clinical Laboratories

Current CLIA competency assessment regulatory requirements: 42 CFR 493.1413(b)(8) and 42 CFR 493.1451(b)(8)

The regulations require “Direct Observations” of routine patient test performance including patient preparation, if applicable, specimen handling, processing and testing and performance of instrument maintenance and function tests.

CMS has defined direct observation as meaning in-person observation.

Virtual Competency Assessments in Clinical Laboratories Questions for Discussion

Would CLIAC recommend greater flexibility in regulatory interpretation to allow for virtual competency assessments in the laboratory setting?

- What is the risk of losing direct in-person observation?
  - How important are the background noise, odors or other activities to a competency assessment?
- What are the recommended limits of virtual competency?
  - Specific instrumentation and capabilities like the product demonstrated?
  - Workload limits on the number of people who can be assessed in a given day?
  - Should we create on-site regulatory requirements for Technical Supervisors and Technical Consultants?
  - Should this be a test-specific flexibility?
- What are the benefits of such a flexibility?

Utilization of Remote Technology for Competency Assessments

Leveraging Technology for Remote Assessments

November 7th 2024

Speakers

Michele Klawitter
American Red Cross
Vice President,
Quality Systems

Andrea Noon
American Red Cross
Director,
Training Strategy

Richard Redman
Computer Generated Solutions
Practice Leader,
Human Capital Initiatives

Agenda

- Objective
- Red Cross Journey
- Important Considerations for Virtual Training and Assessments
- RealWear Wearable Technology & Virtual Competency Assessment
- Advantages of Leveraging Technology for Assessments
- Common Questions and Concerns
- Summary

Objective

- We request CMS to consider technology as direct observation for Competency Assessment.
  - CFR 42 Part 493.1451(b)(8)(i) states “Direct observations of routine patient test performance, including patient preparation, if applicable, specimen handling, processing and testing” and 493.1451(b)(8)(iv) states “Direct observation of performance of instrument maintenance and function checks;”
  - We are aware that CMS’s current thinking of “Direct” is the individual performing the assessment is in-person.
- Today we will demonstrate the successful use of technology in our operation.
- https://vimeo.com/user82190953/review/939716490/64b8760009

The Red Cross Journey

Embracing Technology to Unlock the Value of Human Potential

Strategic Intents

- Deliver best-in-class training with technology-enabled, blended learning
- Increase knowledge retention and skill development
- Improve experience of workforce to drive job satisfactions and staff retention

XR	Video	Virtual Instruction	Web Based Training	OJT & Comp. Assessment
				
Collaborative immersive digital environments where the instructor teaches and learners practice procedure simulations.	Multimedia-based content that supports topic within the learning journey used in vILT, WBT, VR, and AR experiences.	Learning experiences facilitated by a virtual instructor using Teams and in the metaverse.	Interactive digital learning consumed during virtual instruction or on-demand.	Training & competency assessment facilitated in person and virtually using fit for purpose technology.

Sea of Technologies that Theoretically Could Be Used

Wearables

Smart Glasses

Smart Watch

VR/mR Headset

Head Mounted
AR Device

Action Cam

Non-Wearables

Webca

Camcorder

Laptop

Tablet

Smartphone

Important Considerations

For Using Technology in Clinical Settings for Competency Assessment & Training

Form Factor

- Wearable and handsfree
- Compatible with PPE
- Can be used without interfering with work tasks
- Does not cause disruption to others
- Withstands cleaning/sanitization (e.g., IPA)

Functionality

- Stream high-definition video (minimum 720p) and high-quality voice
- Toggle between noise cancellation and sound pass through
- Adjustable camera and mic position
- Optical zoom for best ergonomic experience
- User authentication and security

Connectivity

- Wireless connectivity to the internet – no physical connection
- Bluetooth capable for peripheral hardware such as earphones

xR/AR Capable

- Capture digital artifacts for compliance and record retention
- Annotate/augment video capture with directions/guidance

Assisted Reality (AR) - Realwear Navigator

American Red Cross

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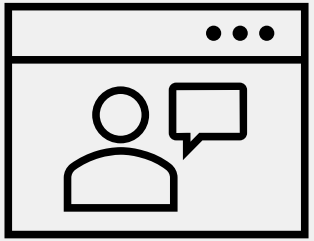
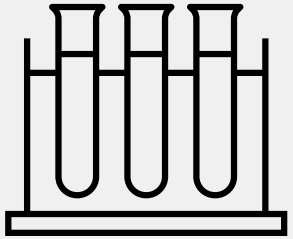
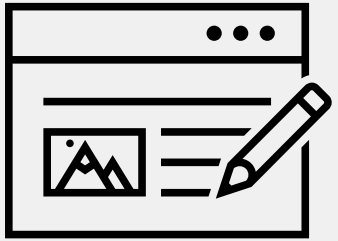
Overview of the Competency Assessment



Connect with your Assessee



Complete Direct Observation



Document ACA Completion

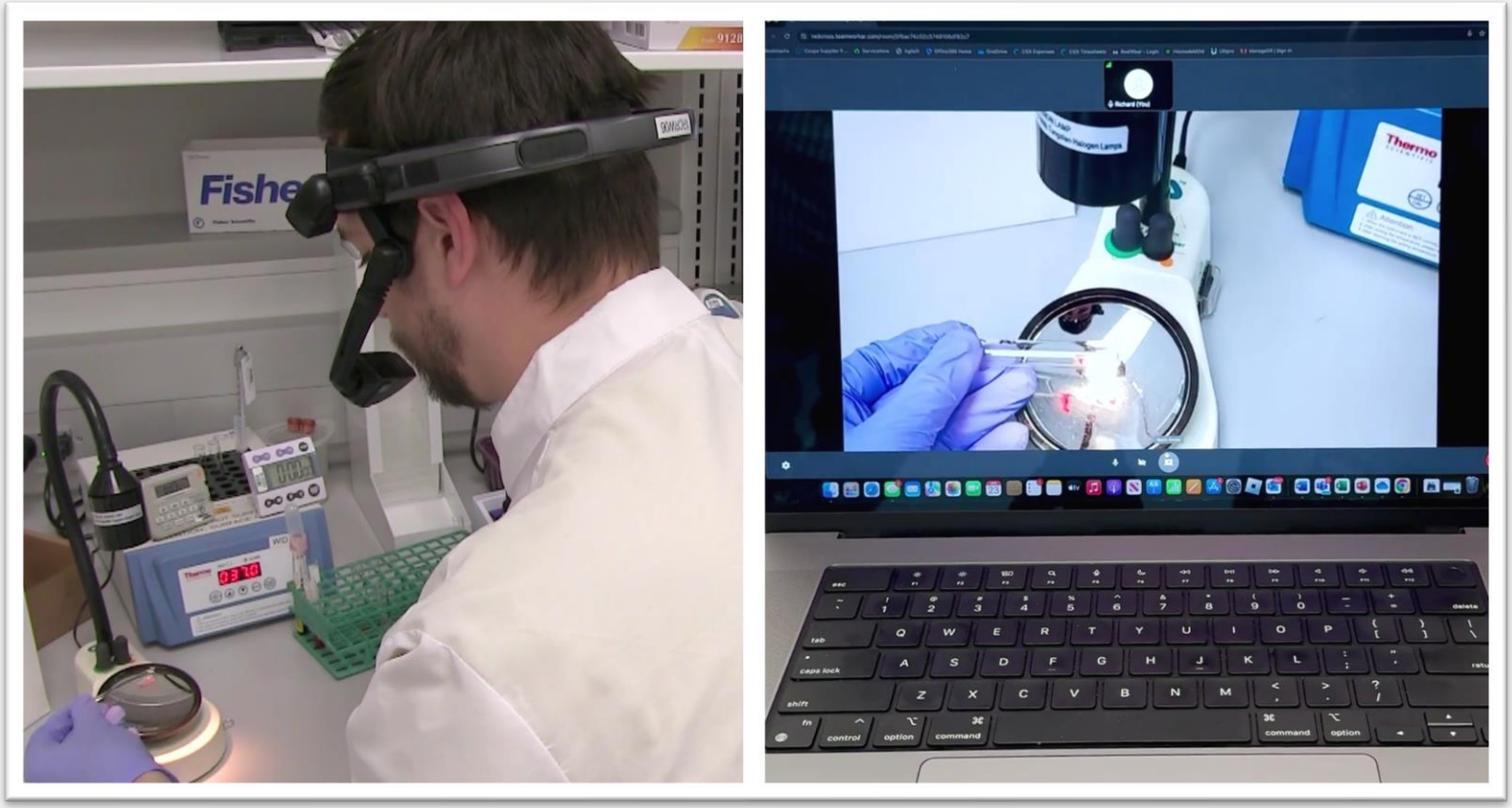
The acceptable performance method of *Direct Observation* can be achieved with this device, including the observing the following procedures: routine patient test performance; monitoring the recording and reporting of test results; performance of instrument maintenance and function checks. *ARC SOP REF-0001548*

Assessor Responsibilities – During the vACA

1. **Invite the Assessee** to the session using their email address (the PIN is sent by the system to the session).
2. **Complete Direct Observation** of the assessee performing required procedures and processes for the designated checklist(s).
3. **Capture documentation** required for CLIA assessments produced by the assessee during the ACA for record retention.

Advantages of Leveraging Technology for Assessments

A less intrusive, first-person view is a significant benefit



Common Questions and Concerns

Q: What if the technology doesn't work or has poor connectivity?
A: Enough time should be scheduled before due date to account for unexpected situations, to troubleshoot and can always be completed in-person.

Q: How do you confirm the identity of assessee?
A: Connection is established via secure PIN delivered within the framework of single sign-on (SSO) network/email.

Q: How clear is the visibility for the assessor?
A: There are network bandwidth requirements to ensure strong connection and streaming capacity. The camera can zoom in / out and has a light.

Q: Can you document steps/tasks being observed?
A: The device being worn and the session for the assessor can capture video and screen images for documentation as needed.

Q: How would virtual assessments account for the day-to-day disruptions that staff experience?
A: The assessee remains in the live environment and are immersed in the typical lab experience. The assessor can be in a more focused setting without disruptions.

Summary

We would like to thank you for taking the time to allow us to present this topic.

The Red Cross is eager to partner with CMS to lead the way in leveraging technology to ensure conformance with CLIA regulations.

Thank you

American Red Cross

Addendum 3

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

Meeting Public Comments

November 6-7, 2024

Atlanta, Georgia

COLLEGE of AMERICAN PATHOLOGISTS

CLIAC Meeting November 2024

CAP Statement regarding Cybersecurity Requirements in the Clinical Laboratory

The College of American Pathologists (CAP) appreciates the opportunity to provide written comments to the Clinical Laboratory Improvement Advisory Committee (CLIAC). As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

The CAP strongly supports efforts to protect health data and continuity of care from cybersecurity attacks and understands the need for policy solutions. Cybersecurity attacks can and do affect every entity in the healthcare community. Hospitals, medical practices, laboratories, patients, and private and public payors all must exchange health data with each other to diagnose, treat, and report diseases. This data is critical to patient care, but also very valuable to bad actors should it fall into the wrong hands.

Adding cybersecurity requirements to the CLIA regulations is both an incorrect and insufficient approach. CLIA is intended to regulate the core functions of the clinical laboratory. Regulatory requirements beyond oversight of laboratory certification and testing would be out of scope. Additionally, government agencies such as the Food and Drug Administration (FDA) and the Cybersecurity and Infrastructure Security Agency (CISA) are working to establish regulatory requirements. These would protect individuals, specify the defensive measures that covered entities need to implement, and outline the responsibilities of covered entities in case of cybersecurity attacks. Effective policy to thwart cybersecurity attacks entails an all-of-Health and Human Services, or even all-of-government approach, working in concert with all-of-industry working collectively. These efforts must include funding support for implementation of new security measures and ensure consistency across government agencies' requirements.

Laboratory systems, including Laboratory Information Systems (LIMS), are connected to and a part of wider systems in hospitals. Data is and must continue to be exchanged between ordering physicians, laboratories, patients, and when appropriate, public health authorities and payors. Each of these actors has a role to play in securing health data. Data is not siloed, and cybersecurity solutions should not be, either. Continuing to address cybersecurity in a piecemeal fashion, singling out individual industries or actors, will not increase security of our health data. Effective solutions will entail rules and standards for preventing and addressing cybersecurity incidents developed and implemented by governments working with all stakeholders.

College of American Pathologists
1001 G Street, NW, Suite 425W
Washington, DC 20001
202-354-7100

The CAP requests that CLIA, or CMS more widely, undertake study and discussions with the laboratory community to understand cybersecurity concerns and the gaps that could be addressed with regulatory action.

For laboratories, one of the most significant risks is documenting that they have received orders once systems go down or are unable to be accessed. Some redundancy should be encouraged, while not being too prescriptive. This could entail parallel, or backup systems, involving paper-based orders and records. Any guidance should be system-wide, constructive rather than punitive, and include a timeframe for integrating paper-based records into electronic systems. Federal funding should be included to help laboratories implement the technology needed for compliance, as cost is the largest barrier to laboratories updating their information technology systems.

Once again thank you the time to discuss the CAP's concerns and recommendations and we welcome the opportunity for further dialogue. Please contact Andrew Northup at anorthu@cap.org or 202.297.3726.

Closing,

The College of American Pathologists

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COLLEGE of AMERICAN PATHOLOGISTS

CLIAC November 2024

CAP Statement on Proficiency Testing: Determination of Clinically Relevant Range of Values

The College of American Pathologists (CAP) appreciates the opportunity to provide written comments to the Clinical Laboratory Improvement Advisory Committee (CLIAC) regarding the terms “clinically relevant values” and “full range of values” as they relate to proficiency testing (PT) in the CLIA regulations. As the world’s largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

As stated in the Code of Federal Regulations, the terminology used is “clinically relevant range[1]”, “full range of values[2]” and “full range of interpretation that would be expected in patient specimens[3]”. As written, the variation between these terms invites confusion. However, we urge CLIAC engage in robust discussion to understand the needs and considerations of laboratory stakeholders, and to share a clear vision of the agencies’ intent regarding revising CLIA’s language around range of values.

While the CAP supports increased clarity in the range of values for PT, the details become much more complicated. Complications to consider include potential manufacturing limitations, clinical utility of the test, assay harmonization status, lack of globally accepted reference intervals, cost, and impact on PT performance. Otherwise, the PT challenge risks inadvertently becoming a problematic exercise with limited value to laboratory participants.

About 500 physicians and doctoral scientists with expertise in pathology and laboratory medicine serve on the 29-discipline specific scientific committees within the CAP. In their advisory role, our members oversee, review anonymous PT performance data, write scientific discussions when applicable to educate laboratory personnel, and set specifications and targets for the CAP PT programs. When writing PT specifications, consideration is given based upon clinically relevant ranges and values, availability of appropriate materials our expert members feel are most important for ensuring appropriate high quality patient care, and compliance with the regulatory requirements listed in Subpart I.

Occasionally, for certain analytes, it is difficult to offer a challenge at the lowest end of the reference range due to manufacturing limitations. Additionally, many routine analytes have negligible clinical significance at low concentrations (e.g., aspartate aminotransferase). Our committee members, most of

[1] Subpart I Proficiency Testing Programs for Nonwaived Testing
[2] § 493.937 Toxicology and § 493.941 Hematology
[3] § 493.959 Immunohematology

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whom serve as laboratory directors, set specifications for PT samples that would be expected in clinical specimens and are keenly aware where medical decisions are made. It is also worth mentioning that it becomes exceedingly difficult to offer an analyte at the low concentration when the regulations do not allow fixed limits with fixed percentage units, so PT providers could use the acceptance limit, whichever is greater/more tolerant.

A couple of examples with manufacturing limitations, or lack of clinical utility:

- Offering artificially low prothrombin time (PT) or activated partial thromboplastin time (aPTT). The CAP Hemostasis and Thrombosis Committee deems such low levels as having no clinical utility in challenging the lower end of the PT or in aPTT reference intervals, and such low values are mostly caused by laboratory artifacts. From manufacturing standpoint, it is challenging to create a sample with abnormally short PT or aPTT time (in seconds), as it would be of concern that manipulation would make the proficiency testing sample unsuitable and potentially ungradable, as experienced few years back in the CAP Coagulation PT Program. Manipulations of plasma to achieve such low levels is also very costly with no added value to participants. Additionally, in the context of lack of assay harmonization or globally accepted reference intervals, proficiency testing samples that challenge the low end of the range for one assay may not recover similarly across all assays. Such differences in PT performance are likely due to sample variation secondary to the manufacturing process rather than a reflection of meaningful laboratory testing performance differences, and as such, it becomes burdensome for laboratories as they are required to perform alternative performance assessment when a PT provider is unable to formally grade/evaluate a challenge.
- Another example that has presented manufacturing limitation is to offer T3-Uptake on the low end of the reference range. Even at the endogenous levels, addition of buffer, pH solutions, background analytes increase the T3-Uptake values, rendering the challenge as not meeting the regulatory requirement. Of the fifteen challenges offered throughout the year, every effort is made by the CAP to challenge the laboratories in covering the clinically relevant range of the analyte values expected in patient specimens.

We hope that broader, robust discussions with key stakeholders and PT providers will be held prior to advancing proposed regulatory revisions on this important issue. The CAP stands ready to contribute our scientific knowledge and real-world experience to such discussions.

Once again thank you the time to discuss the CAP's concerns and recommendations and we welcome the opportunity for further dialogue. Please contact Andrew Northup at anorthu@cap.org or 202.297.3726.

Closing,

The College of American Pathologists

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American Proficiency Institute

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STATEMENT TO THE CLINICAL LABORATORY IMPROVEMENT ADVISORY COMMITTEE
November 7, 2024

Range of Values for Proficiency Testing Samples

Mr. Chairman, members of the Clinical Laboratory Improvement Advisory Committee, my name is Sue Harmer and I am President of the American Proficiency Institute (API). Established in 1991, API is one of the nation's largest, accredited proficiency testing providers, serving over 20,000 hospital and physician office laboratories. Thank you for this opportunity to speak with you today as you consider issues related to the determination of clinically relevant ranges of values for proficiency testing samples.

My comments focus on how to ensure proficiency testing providers are covering the appropriate range of targets. Simply put, there are two ways to calculate the target value for each analyte tested – "All-Participants" means and "Peer Group" method-specific review.

With the All-Participants measure, the target value is an average of all the various methods used by all proficiency test participants for a particular analyte. The average is then used to determine the range of acceptable results for each analyte in a sample. However, since one or more large peer groups may recover significantly lower or higher than other methods, the All-Participants mean may be biased.

Alternatively, for a Peer Group measure, data is grouped and examined by reagents or instruments for a particular analyte tested. This measure is more feasible for certain analytes, especially the newly regulated cardiac markers. Peer Group measures are often used instead of All-Participants because proficiency testing results may be subject to a matrix effect. An example of a matrix effect is when the presence of substances in a sample, other than the intended analyte, may affect the quantification of the intended analyte. A matrix effect can impact each methodology differently but those using the same methodology are affected similarly, which adds to the importance of grading by peer group.

Thirty-plus years ago, All-Participants means was written as the default for CLIA proficiency testing measurement, but Peer Group measures were permitted when necessary. Today, Peer Groups measurement is the default for proficiency testing providers as the importance of matrix effects has been acknowledged and the sheer number of methods makes it impractical to review and document bias or matrix effects for every method.

The July 11, 2022, final rule on proficiency testing regulations recognizes this by stating, "peer grouping is generally the way that target values are set for most analytes." The resulting §493.2, now includes a definition of peer group and a broader use of peer groups in a revised definition of target value. The target value definition now states, "If the peer group consists of 10 participants or greater," the target value is the "mean of all participant responses after removal of outliers;" "the mean established by a definitive method or reference methods;" or "the mean of a peer group…." All-Participants means would be required when a peer group consists of fewer than 10 participants.

To highlight how the measurement method impacts the averages and range of values obtained, take a look at prothrombin time. Results from different prothrombin time methods are not comparable, and this difference is magnified when testing proficiency testing samples. The first chart below shows the All-Participants averages for all 2023 proficiency testing samples from API.

Test Event	All-Participant Means				
2023 1st Test Event	11.4	11.8	19.5	32.0	39.7
2023 2nd Test Event	11.0	11.1	11.9	28.8	45.7
2023 3rd Test Event	11.0	11.1	11.7	11.9	45.7

This All-Participants data was reviewed to determine whether API had offered challenges covering a reference range of 9.4-12.5 seconds. Using the data above, it appears we did not challenge the low end of the reference range. If the data is grouped by method (as in the chart below), you can see that method bias in the All-Participants data obscures how low the results were for many participants.

The chart below shows the spread of values reported by different methods on one sample with an All-Participants mean of 11.0.

Peer Group (# participants)	Lowest Result	Mean	Highest Result
Reagent A (1250)	8.7	10.3	11.5
Reagent B (25)	10.1	10.8	11.3
Reagent C (600)	9.8	10.9	12.0
Reagent D (30)	10.0	11.2	12.1
Reagent E (500)	12.0	12.9	14.7

This data shows three peer group means were lower than 11, and two were higher – one significantly higher. The significantly higher group represented 24% of all participants, and raised the overall mean so much that it appeared a low target had not been provided. In fact, over half the participants, those using Reagent A, had a target value of 10.3, and approximately half of those participants reported values lower than 10.3. The lowest acceptable results reported in that Reagent A peer group were lower than the requested All-Participants reference range.

The All-Participants data at low or high levels can be skewed, not meeting the 80% consensus requirement for evaluating participant results. In the instance above, Peer Group data should be used to determine whether the reference range for prothrombin time is covered by a proficiency testing program.

Another technical matter impacting proficiency samples addresses how some targets may not be achievable in manufactured samples. A leading provider of hematology samples, known for its expertise in cell stabilization, explained the technical limitations of proficiency samples for white blood cell (WBC) differentials in a 2022 open letter: "Proficiency products are manufactured from multiple donors. When the donor cells are stabilized and pooled, they become very uniform in ratios for the differential. Due to the overall similarity of donors that make up the stabilized cellular material, the differential can only be altered slightly (15-40% lymphocytes, 50-75% neutrophils) to maintain manufacturable product. Stabilized proficiency materials can produce anomalous results when differential populations are varied at extreme (abnormally high or low) levels… it is not achievable for WBC differentials in stabilized proficiency products to represent the full range of values expected in patient results."

To address these, and other, issues related to the range of values for proficiency testing samples, we offer the following suggestions for your consideration:

1. For a more impactful data review, it may be useful to know which analytes are best summarized through Peer Group data. It is reasonable to recommend that proficiency testing providers list up front each analyte for which Peer Group data is preferred.

2. There should be recognition that proficiency testing results vary from results on patient samples, due to matrix effects. This is common when using a manufactured sample as pooled plasma is frequently used, there may be stabilizers or preservatives present, or multiple analytes may be targeted in the sample.

3. To better ensure a broad range of targets, it would helpful if proficiency testing providers were provided with the desired ranges for each analyte further in advance. The current annual approval process allows limited time for research and development activities that might allow the desired reference ranges to be met. Providing the desired ranges for each analyte in advance would also allow proficiency testing providers an opportunity to provide feedback on challenges that may arise from manufactured samples.

On behalf of API, thank you for your consideration of these comments. I would be pleased to answer questions or provide additional details.

COLLEGE of AMERICAN PATHOLOGISTS

CLIAC November 2024

CAP Statement on the Utilization of Remote Technology for Competency Assessments

The College of American Pathologists (CAP) appreciates the opportunity to provide written comments to the Clinical Laboratory Improvement Advisory Committee (CLIAC). As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. The CAP supports CLIAC's interest in reducing the burden of Competency Assessment (CA).

Competency Assessment is a critical piece of ensuring laboratory quality, requiring pathologists in the role as laboratory director to manage and track the qualifications, continuing education, and assessments for the laboratory staff they oversee. In the case of large laboratories or when one individual serves as laboratory director for multiple laboratories, satisfying the current CA requirements can take up a significant portion of their time, taking their attention away from patient testing and diagnosis. CAP Accreditation has not detected quality issues originating from the current CLIA CA requirements. Thus, the CAP supports the current scope of Competency Assessment under CLIA, believing that expansion could have negative consequences in terms of staff burden and burnout without an upside of quality improvement.

The six required elements of competency assessment for nonwaived testing include:

1. Direct observations of routine patient test performance, including, as applicable, patient identification and preparation; and specimen collection, handling, processing, and testing.
2. Monitoring the recording and reporting of test results, including, as applicable, reporting critical results.
3. Review of intermediate test results or worksheets, quality control records, proficiency testing results, and preventive maintenance records.
4. Direct observation of performance of instrument maintenance and function checks.
5. Assessment of test performance through testing previously analyzed specimens, internal blind testing samples, or external proficiency testing samples.
6. Evaluation of problem-solving skills.

All but the two elements requiring direct observation may already be done remotely. Direct observation can also be done remotely, as was demonstrated during the Public Health Emergency (PHE) remote assessments proved to be practical and adequate. The requirements outlined in CMS's remote survey process during the Public Health Emergency (PHE)could inform the development of permanent policy for remote competency assessment.

College of American Pathologists
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202-354-7100

From a technical perspective, conducting direct observation remotely is entirely feasible. The CAP and other accreditors conducted some inspections remotely using off-the-shelf technology. The CAP found that conducting remote assessment via video calls on a mobile device, for example a laptop on top of a wheeled cart, or a smartphone mounted on a tripod, provided enough sight of the laboratory work being done to satisfactorily assess competency.

Enabling assessments to be done remotely, without a supervisor traveling, and without laboratory personnel modifying their workday and workflow to accommodate an additional person in the laboratory will same time and resources while still upholding quality standard. Small rural hospitals or clinics where there is a single technologist working may benefit the most from this possible option. To maximize the benefits of moving to remote observation, the technology involved must be readily available, affordable, and easy to implement in the laboratory.

Requirements for remote observation of competency assessment should be developed using a consensus-based approach to gain a solid understanding of CLIA's goals and the capabilities and challenges specific to current laboratory practice. One of the challenges might be ensuring that the competence records are maintained and available at the location with that CLIA number so that all records are available for inspections. To identify suitable technology tools for conducting remote assessments, CMS should clarify what is needed to be viewed on screen, if it needs to be from a 1st-person vantage point, and when CA is done using real patient samples, considerations would need to be made around how protected health information is viewed and stored.

Once again thank you the time to discuss the CAP's concerns and recommendations and we welcome the opportunity for further dialogue. Please contact Andrew Northup at anorthu@cap.org or 202.297.3726.

Closing,

The College of American Pathologists

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Statement to the Clinical Laboratory Improvement Advisory Committee

By the

American Association for Laboratory Accreditation (A2LA)

November 7, 2024

The American Association for Laboratory Accreditation (A2LA) appreciates the opportunity to provide comments to the Clinical Laboratory Improvement Advisory Committee (CLIAC) for your consideration.

A2LA has been offering accreditation services for over forty-five years. We currently hold Centers for Medicare and Medicaid Services Deemed-Status and the International Laboratory Accreditation Cooperation (ILAC) Recognition to provide clinical laboratory accreditation. A2LA is the only accreditation organization in the world to achieve and maintain both of these formal recognitions.

Over the years, A2LA has performed thousands of remote assessments in different capacities and has gained valuable knowledge of the remote assessment process. We wish to highlight some points for your consideration that may make virtual competency assessments more widely accepted.

A primary objective when performing a remote assessment is that the assessment is held to the same level of rigor as an in-person assessment. A2LA uses resources provided by ILAC in order to help us meet this objective.

A2LA considers if an assessment activity is a candidate for a remote assessment, by first ensuring that the laboratory is eligible for a remote assessment by following the remote assessment policy which includes conducting a risk assessment. A risk assessment is an important tool that should be included in a laboratory's policy and/or procedures for a virtual competency assessment. A risk assessment is the overall process of risk identification, risk analysis, and risk evaluation (according to ISO 31073:2023) and is initiated early in the planning stages. The concept of a risk assessment should be applied to competency assessments in order to determine if a virtual competency assessment is viable.

For example, for an accreditation organization conducting a survey, A2LA considers these factors in a risk assessment: previous survey technique (remote or in person), number and nature of previous findings, depth of previous survey observations, laboratory scope, and laboratory resource changes from previous survey. Likewise, the risk assessment factors for competency assessments may include technique for previous competency assessments, environmental conditions, outcomes/findings from previous competency assessments, external survey results for that area and severity of findings, proficiency testing results, and staff turnover. Another factor that needs to be considered is if there are areas of the laboratory in which the testing would not be able to be easily observed due to internet connectivity issues or the lack of visibility of the testing personnel, facilities and/or instruments. An additional factor one needs to consider is the media that the laboratory records are maintained - electronically or paper, and how readily are they available for review. This may lead to a higher risk of the competency assessment not being held to the same standard as an in-person assessment. With a higher risk identified, the

laboratory may decide that an in-person competency assessment is a better option than a virtual competency assessment. Alternatively, if the laboratory considers this to be a lower risk, the laboratory will need to develop a mechanism to share necessary records prior to the virtual competency assessment occurring. This may significantly increase the amount of preparation and overall time in which a competency assessment occurs.

A2LA encourages the committee to consider these topics as CLIAC continues to evaluate the use of virtual competency assessments.

Thank you for allowing A2LA the opportunity to provide comments on this matter and consider us as a resource if additional information is required.

Addendum 4

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

Meeting Transcript

November 6-7, 2024

Atlanta, Georgia

November 6, 2024

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

CLIAC CHAIR: Well, good morning, everyone, and welcome to the Fall 2024 Clinical Laboratory Improvement Advisory Committee, CLIAC Meeting. My name is Jordan Laser, and I'm the Chair of CLIAC. Before we get started, I'd like to take a few minutes to recognize Dr. Collette Fitzgerald, who will be rolling off as CLIAC CDC Ex Officio. So Dr. Fitzgerald was appointed to clinic as the CDC Ex Officio member in 2018. She provided the committee with 12 CDC update presentations. And during her tenure as CDC Ex Officio, there have been 109 CLIAC recommendations and seven CLIAC workgroups. Dr. Fitzgerald is now the Acting Associate Director of Science for the CDC Office of Laboratory Systems and Response. And on a more personal note, I want to thank Dr. Fitzgerald for her support of CLIAC, as well as her support and encouragement during my onboarding and time as chair. So we thank Dr. Fitzgerald for her service and commitment to CLIAC. I'd also like to recognize Dr. Ren Salerno, who was appointed to CLIAC as the Designated Federal Officer in 2018. He served as a CDC-- CLIAC CDC Ex Officio from 2016 to 2018. And during his tenure on CLIAC, there have been 118 CLIAC recommendations and seven CLIAC workgroups. Ren has recently been appointed the Director of CDC's office of the Laboratory Systems and Response. And also on a personal note, I want to thank Ren for guiding me throughout my time as chair. His insight and advice has always been really meaningful, and certainly has enabled CLIAC to be as effective as possible. So I'll turn it over to Ren to say a few echoing words.

DR. REYNOLDS SALERNO: Thank you, Jordan. Wow, what a day. And very sad for me to be saying goodbye to CLIAC-- and it's probably the wrong way to say it because although I'm giving up my official duty on CLIAC, I remain a huge supporter and believer in the importance of CLIAC. I'm incredibly grateful to current members, former members of CLIAC. I've developed an incredible-- expanded my network of colleagues across the clinical laboratory community thanks to CLIAC. Many current and former CLIAC members have been mentors for me. Many are now close friends of mine and people that I rely on deeply to help me do my job, but also just to enjoy my life. And so just wanted to emphasize how much I appreciate all of you. All of you who cares as much and probably a lot more than I do about clinical laboratory medicine and the importance of laboratory quality in clinical diagnostics. And that the one thing I can assure you is that in my new role at CDC where I'm now the single point of accountability for all CDC laboratory activities, I will continue to rely on the wisdom of members of the clinical laboratory community and continue to bring that particular perspective to CDC and to public health. So thank you very much for almost nine years of work on CLIAC. I think you're in incredibly strong hands with Heather as the new CLIAC Designated Federal Officer. Hopefully you all already understand that Heather runs these meetings-- has been running these meetings anyway, so essentially nothing will change there. As well as Victor as the new Ex Officio for CDC. So Thanks so much. I appreciate these few minutes having an opportunity to express my appreciation to CLIAC.

CLIAC CHAIR: Excellent. Thank you.

CLIAC DFO: Thank you Ren. So with that, my name is Heather Stang. I'm the Senior Advisor for Clinical Laboratories. Here in the Division of Laboratory Systems in the Office of Laboratory Systems and Response at CDC. And, as I announced, I am the new Designated Federal Officer of CLIAC. The CDC manages clinic and provides scientific and technical advice and guidance to the Department of Health and Human Services. The advice and guidance CLIAC provides to HHS focuses on issues related to the 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 CLIA standards. As this is a Federal Advisory Committee meeting, the Zoom chat and Q&A functions have been disabled for the online audience members. If you are experiencing Zoom difficulties, please get in touch via email at cliac@cdc.gov.

CLIAC CHAIR: Yes. Members are reminded of the importance of attending the entire meeting, and, of course, returning promptly from breaks to ensure a quorum, until all matters before the committee are addressed and the meeting is adjourned. We will have recommendations. Our official recommendations are those related to a topic on the meeting agenda that is put forward a motion, seconded by another CLIAC member, and voted on by clerk to obtain a majority vote. A reminder that all CLIAC discussions and deliberations must be available to the public, and accordingly, the chat function is not available for public viewing. And CLIAC members should refrain from engaging in topic discussions offline through the chat function. Please use the chat only to notify me of your desire to comment, during the discussions, or ask a question of the speaker. Alternatively, and preferably, feel free to raise your virtual hand in Zoom as it actually places you in order for questions or comments. And an email to Heather is another option for submitting draft recommendations as well. The CLIAC recommendations table is available on the meeting website and contains a list of all past CLIAC recommendations, including information on their implementation status.

CLIAC DFO: So I would like to take this time to recognize outgoing member Miss Heather Duncan. Ms. Duncan's device expertise in industrial food safety, clinical laboratory testing, laboratory medicine, regulatory compliance, and quality

assurance provided a very diverse perspective to many CLIAC discussions. She was instrumental in leading recommendations related to the expansion of point-of-care testing during the COVID-19 pandemic, the future of laboratory medicine, and non-traditional testing sites, efforts to address public health and clinical laboratory workforce challenges, the laboratory's role in advancing health equity, and efforts to address the CLIA top 10 deficiencies. Ms. Duncan graciously served as Chair of the CLIAC/CLIA Certificate of Waiver and Certificate of Provider Perform Microscopy Workgroup and also served as a member of the CLIAC Biosafety Workgroup. Please visit the CLIAC meeting website for a detailed list of Heather's contributions to clinic. Heather, we thank you for your service to the committee. And I will pull up the roster slide next, and we will go through that. So in addition to myself and Victor, we have three new members joining CLIAC-- Dr. Olga Ceron, Soojin Jun, and Dr. Anthony Tran. All new and current members will provide an introduction as we make our way down the roster for acknowledgments and introductions. Please follow the roster, slide on the screen, introduce yourself, and provide any required public disclosures and conflicts when we reach your name. So, again, I am Heather Stang. I am serving as the CLIAC DFO, and I have no conflicts of interest.
DR. JORDAN LASER: Yes, hi, how are you? Jordan Laser. I'm the Senior Director for Clinical Medical Affairs at a company called Bio-Techne. In terms of conflict of interest, I'm both employed and have stock in Bio-Techne, and I serve as roles and committees in the College of American Pathologists, as well as the Association for Molecular Pathology. Thank you. Esther?

DR. ESTHER BABADY: Yes. Hi, everyone. I'm Esther Babady. I'm The Chief Of Clinical Microbiology at Sloan-Kettering Cancer Center in New York City. In terms of conflict of interest, I serve on the Executive Board of the American Society for Clinical Virology, as well as some committee for the Association of Molecular Pathology and the American Society for Microbiology. I also receive research funding from a couple of commercial entities, including Roche and Copan and Altona Diagnostics.

MR. MICHAEL BLACK: All right. My name is Mike Black. Good morning, everyone. Certainly glad to be here. I'm currently the Vice President of Ochsner Health Laboratories, and I do not have any conflicts of interest. Thank you.

CLIAC DFO: Chester is unable to attend for this meeting, so we will move on to Olga.

DR. OLGA CERON: Good morning, everyone. I'm Olga Ceron. I'm a board-certified ophthalmologist, retina specialist. I currently work at Astellas Pharma as a development physician, and also a practicing physician at the Joslin Diabetes Center in Boston, and serve as an examiner for the American Board of Ophthalmology as a mentor as well for the American Academy of Ophthalmology. And excited to be part of this great team and look forward to working with everyone.

DR. KIMBERLE CHAPIN: Good morning, everyone. Happy to be here. Thanks so much to Reyn and Colette for their past duties. I will miss them personally, they've been awesome. I am the Chief Medical Officer for a startup called deepull, which is in Barcelona, Spain. And I-- that's my conflict. I'm still a professor at Brown Medical School in pathology and medicine.

CLIAC DFO: James.

CLIAC CHAIR: It looks like we're having some audio trouble. I see he's unmuted, but we can't hear him. Yeah, we still can-- OK, we'll, come back.

CLIAC DFO: Heather.

MS. HEATHER DUNCAN: Hey, I'm Heather Duncan. I'm the Director of Lab Services at ECU Health. I have no conflicts to disclose today, and it has been my great pleasure privilege to serve with this group. Thank you.

DR. MARY EDGERTON: Hi. It's great to have the opportunity to be with you all one more time. I'm Mary Edgerton. I'm an AP/CP board-certified pathologist specializing in breast pathology at the University of Nebraska Medical Center. And I'm also boarded in clinical informatics.
DR. TANNER HAGELSTROM: Good morning. Good morning. My name is Tanner Hagelstrom, I'm the senior laboratory director for Natera, an oncology business unit. I'm a molecular geneticist and cytogeneticist. I also am the founder of a company called Expectant Diagnostics, and I own stock in both the Natera and Expectectant. Thank you.

CLIAC DFO: We'll go back to James, see his hand up.

DR. JAMES CRAWFORD: Presumably you can hear me now. So I'm Jim Crawford, Professor and Chair Emeritus of Pathology and Lab Medicine at Northwell Health. My disclosure, I'm Chair of the Board of Directors of Project Santa Fe Foundation, an educational foundation. A non-voting member of Clearpath, which makes robotic microtome. President of Northwell Health Genomics Alliance. And I receive funding from the National Cancer Institute.

DR. YAEL HEHER: Hi, good morning, everyone. I apologize for my camera. I'm traveling for family reasons today, but it's an honor to be here once again. Heather, so glad you're formally in this role. Welcome. And thanks, Reyn and team, for your service. I am a renal pathologist. My clinical work is at Boston Children's Hospital, but my main job is that I'm the Chief Quality officer for Beth Israel Lahey Health, a 14-hospital health system in Boston, Massachusetts and New Hampshire. And in that role, I oversee quality for the system, and I'm also the executive that oversees labs for the system. So hi, Olga, welcome. Oh, Joslin's part of our family.

CLIAC DFO: Mary, I see your hand up. Did you forget something you wanted to disclose?

DR. MARY EDGERTON: Yes. I just signed an agreement to be a consulting panelist for AstraZeneca on HER2 new staining interpretation. I forgot about it.

DR. YAEL HEHER: And I should add, I have nothing to disclose.

CLIAC DFO: Perfect. OK, Soojin.

DR. SOOJIN JUN: Hi, my name is Soojin. I'm a board-certified geriatric pharmacist. I'm very happy to be here as a new member. Thank you so much for including me. I do not have any conflicts of interest. To add, that I'm also a patient safety activist, co-founder of an organization called Patients for Patient Safety US under the umbrella of WHO. Thank you.

DR. DAVID KOCH: Yeah, good morning, everyone. Nice to be here. I am the Professor of Pathology and Laboratory Medicine at Emory University in Atlanta, and also director of clinical chemistry at Grady Memorial Hospital in Atlanta. And I have nothing to disclose.

DR. HUNG LUU: Good Morning. I am a Professor of Pathology at UT Southwestern Medical Center and a hematopathologist, and I also serve as Director of Clinical Pathology at Children's Health, a pediatric health care system in North Texas. And for disclosures, I am active in the CIP in committees. And I also receive salary support from the FDA and the VA for various initiatives for the Shield Project. And I'm also on the Clinical Advisory Committee for Health Gorilla with stock options.

DR. NIRALI PATEL: Hi. Nirali Patel. I'm Vice President of Molecular Pathology at Tempest AI, and I also serve on the Board of Directors of COLA, a CMS-deemed accreditation organization, and have no other conflicts to disclose.

DR. MICHAEL PENTELLA: Good morning. I'm Mike Pentella. I'm the director of the State Hygienic Laboratory at the University of Iowa. I'm also a clinical professor in epidemiology. I'm active in the Association of Public Health Laboratories. And I'm board-certified in medical microbiology. Nothing else to disclose.

DR. ANTHONY TRAN: Good morning. Tony Tran, I am the State Public Health Lab Director in California, as well as I lead the Center for Lab Sciences within the California Department of Public Health. Like Dr. Pentella, I'm also active in the Association of Public Health Laboratories, serving on the Board of Directors, as well as committees, and also subcommittees and working groups within the American Society for Microbiology. Thank you.

DR. J. MARK TUTHILL: Hey, good morning, everybody. It's Mark Tuthill. I am the Division Head of Informatics at Henry Ford Health System. I have no financial disclosures, but I am a member of the Association of Pathology Informatics Executive Board and direct their annual conference that will be held this year in Ypsilanti, Michigan, so come join us.

DR. R.W. WATKINS: Well, there had to be one in there. Chip Watkins. I think this is my last rodeo with CLIAC and I'm happy to be back. I'm a family doc, over 35 years of experience as a family doc. I am also a Lab Director and Chief Medical Officer of a small lab here in Asheville, North Carolina. You may have heard about Asheville over the last couple of weeks. I'm also on the COLA Board of Directors, and then work with a group called Community Care of North Carolina where we work with particularly independent practices and helping them stay competitive with larger systems. Thank you. No conflicts.

MS. APRIL VEOUKAS: Hello. My name is April Veoukas, and I'm the AdvaMed liaison representing the AdvaMed Medical Technology Trade Association, which includes in vitro diagnostics. I'm an employee of Abbott, Director of Regulatory, and have financial and stock interest in Abbott, which, among our product portfolio, includes in vitro diagnostics and laboratory services.

DR. VICTOR DE JESUS: Good morning, everybody. I am Victor De Jesus. And I currently serve as the Acting Director-- I have no financial disclosures, but I do serve as a member of the Consensus Council of the Clinical and Laboratory Standards Institute. Thank you.

MR. GREGG BRANDUSH: Good morning, everyone. My name is Gregg Brandush. I'm the Director of the Division of Clinical Laboratory Improvement and Quality. I'm also the CMS Ex Officio. And I have no conflicts of interest to report. Thank you.

DR. COURTNEY LIAS: Hi, everyone. I'm Courtney Elias. I am the FDA Ex Officio member, and I'm the Director of the Office of In Vitro Diagnostics at FDA. And I have no financial disclosures to report.

CLIAC CHAIR: Well, thank you, everyone, for the introductions. We'll get underway very shortly, but just a couple of comments about public comments. So during the period dedicated to the committee discussion, participation is limited to CLIAC members only. CLIAC can accept public comments that directly relate to the topics announced in the Federal Register Notice Meeting Announcement. So for this meeting, the committee will discuss and deliberate on the CLIAC Biosafety Workgroup Report, the CLIAC Next Generation Sequencing Workgroup Report, cybersecurity requirements in the clinical laboratory, proficiency testing, determination of clinically relevant range of values, and finally, the utilization of remote technology for competency assessments. So public comment periods are scheduled at the end of each topic area for both meeting days. Today, the public comments will be limited to a total time of five minutes per individual or group. If anyone in the audience wishes to address the committee, the public comment portion of the meeting is the proper forum. If you wish to make a public comment on any of the agenda meeting topics, please email cliac@cdc.gov as soon as possible for inclusion in the public comment period. A little bit about logistics. Copies of the PowerPoint presentations and other meeting materials are posted on the CLIAC website. This meeting is being webcast via Zoom webinar, and we welcome everyone online. Links to this webinar are also provided on the CLIAC website. The meeting is also recorded to assist in preparing an accurate written summary of the proceedings. So why don't we get at it, and we could start today with our agency updates. We'll have updates from the CDC, CMS, and FDA. And we're going to have a little bit of time at the end of each update for a few committee questions, if there are any. After the updates, we'll take our one-hour break and we'll move on from there. So up first is Victor, who's going to be providing us with a CDC update.

❖ Agency Updates and Committee Discussion

Centers for Disease Control and Prevention (CDC) Update
Víctor R. De Jesús, PhD, CDC Ex Officio

DR. VICTOR DE JESUS: Great. Thank you, Jordan. And once again, good morning to all. And Thank you for the opportunity to share our updates this morning on our work in the Division of Laboratory Systems in the Office of Laboratory Systems and Response at CDC. Moving forward, I will refer to our division as DLS for the remainder of the presentation. Next slide, please. Got it? Yes.

So-- sorry, my internet's acting up, of course. So, again, our CDC Director, Dr. Mandy Cohen, has repeatedly and publicly stated that laboratories are core public health infrastructure. Our collective laboratory expertise-- response. The output of our work is a critical, critical piece of the architecture and infrastructure of public health readiness and response. Laboratory systems, which include, of course, quality, safety, informatics, workforce and response readiness, are the fundamental components of our core public health infrastructure. These internal and external laboratory functions are inextricably linked with one another. Next slide, please.

On October 1 of this year, the Office of Laboratory Science and Safety, the Center for Laboratory Systems and Response, the Division of Laboratory Systems, and the Division of Core Laboratory Services and Response were realigned into the Office of Laboratory Systems and Response. So we have been in existence for approximately 36 days. The rationale for the realignment is very clear. CDC needs an organization that demonstrates that laboratories are core public health infrastructure. CDC laboratories, as well as laboratories outside CDC that support public health. Our vision for the realignment is to create one cohesive organization to support and advocate for laboratories and align CDC's cross-cutting laboratory programs with one CDC. Ultimately, our goal is to align internal and external functions, eliminate redundancies, reduce inefficiencies, and improve the coordination and collaboration across our agency, interagency, and with external partners. Next slide, please.

Our mission is to create a core laboratory infrastructure that provides operational and system support to both CDC and the nation's public health and clinical laboratories, thereby ensuring high-quality and safe laboratory science, reliable diagnostics for outbreaks and harmful exposures, as well as developing and encouraging strong partnerships for readiness and response. Next slide, please.

Now onto providing some updates on our activities that support laboratory equality for the nation. Next slide, please.

First, we're happy to report that we have updated our very popular waived testing resources, which include the Ready? Set? Test! educational material. On this slide, you will see the new look and feel of these waive testing resources. The Ready? Set? Test! resource, or RST, includes recommended best testing practices for physicians, nurses, medical assistants, pharmacists, and others testing patients on their CLIA Certificate of Waiver. This new revision includes updated CLIA guidelines, PT referrals for certificate of waiver sites, updated safety recommendations, best quality assessment practices, and updated self-assessment checklists for good testing practices, which were updated for both the Ready? Set? Test! booklet, and also updated language and processes to check through all phases of the testing process. The impact of the laboratory testing community, which includes a highly competent laboratory workforce, cannot be overstated. Over 1,300 RST booklets have been distributed to the laboratory community in FY24. And over 1,000 booklet copies have been downloaded from our CDC waive testing website in fiscal year '24, which just ended at the end of September. Next slide, please.

The next resource that we have updated is To Test or Not to Test, which provides considerations and preparations for performing waive tests. It also assists those implementing-- certificate of waiver requirements for multi-location testing sites. It also includes updated CLIA guidelines on PT referral for certificate of waiver sites, as well as general safety recommendations. Over 600 To Test or Not To Test booklets were distributed to the lab community in fiscal year '24. And over 1,300 copies have been downloaded from our waive testing website during FY24. These continue to be incredibly useful and popular resources that are freely available to the community on our website. Next slide, please.

A brief update on our Next Generation Sequencing Quality Initiative. CDC, the Association of Public Health Laboratories. state and local public health laboratory partners have collaborated on the Next Generation Sequencing Quality Initiative. This initiative is moving forward with a coordinated and comprehensive plan to develop and implement an NGS-focused quality management system that helps to ensure high quality, reliable data for nationwide disease surveillance systems, diagnostic or reference laboratory testing, and other public health actions that help improve patient care and public health outcomes. The initiative is working to harmonize quality standards for NGS across public health and provide laboratories with confidence in the reported results. The initiative is working actively to create a toolkit of resources that NGS testing sites can use as a starting point to help avert duplication of efforts, increase efficiency, and save some cash along the way. The initiative supports NGS activities to meet multiple requirements, including CLIA as a prerequisite for use of this transformative technology in public health, laboratory diagnostics and surveillance activities. The quality initiative regularly refreshes the QMS tools and resources page, maintaining current information across 115 documents per user accessibility and enhanced experience. Since October of 2023, the web pages have amassed over 17,500 views and nearly 10,000 downloads and website visits that have been recorded since 2021. The line graph displays the number of visitors trending upward since 2021 to today. And the histogram provides the top category downloads. And again, the link to the website is at the bottom of the slide. Next slide, please.

I'd like to highlight a couple of recent accomplishments of the quality initiative. And first, I would like to highlight the QMS assessment tool, which is the most downloaded tool on the Resources website. This tool completed its cyclic review in October of 2024. This assessment is a structured workbook with tabs outlining recommended components for each quality system essential, ensuring comprehensive compliance evaluation. It emphasizes next generation sequencing processes within the QSEs or the quality system essentials, integrating advanced technologies into the quality management framework. Next is the Pathway to Quality-Focused Testing, which is an interactive tool that simplifies assay validation and system maintenance by monitoring progress, despite ongoing challenges due to the lack of a standardized quality framework. It integrates the 12 QSEs with CLIA regulations and professional guidelines to ensure robust support for testing implementation. For reference materials, the quality initiative develops these materials to assist laboratories in pipeline development, standardization and reproducibility, enhancing the reliability, accuracy, and consistency of complex genetic data generated by technologies. Currently, the quality initiative has two ongoing pilot studies, developing these reference materials which serve the needs of the sequencing community. And lastly, automated end-to-end sequencing platforms. Clear Labs offers a fully-automated NGS platform designed for the detection of foodborne illnesses. To enhance its functionality, the quality initiative has developed three key documents for this automated platform. The Clear Labs software update form, the Clear Labs DX in-use equipment maintenance log, and the Clear Labs pre-installation checklist. Next slide, please.

Now I'd like to provide a few updates on our activities to support laboratory safety. Next slide.

DLS launched the ECHO Biosafety Program in January of last year to develop and engage a biosafety community of practice to address biosafety challenges in both clinical and public health laboratories. The DLS ECHO Biosafety Program is based on the extensions for community health outcomes model, or ECHO model, developed by the University of New Mexico Health Sciences Center. The main feature of the sessions is the discussion of solutions to address biosafety challenge. The goal of ECHO Biosafety is to bridge gaps, build a community of practice, and enhance biosafety in our laboratories nationwide. The ECHO Biosafety sessions are designed for laboratory biosafety professionals. Since January of last year, 20 sessions have been held and we're currently planning monthly sessions for 2025. Upcoming topics of discussion include biorisk management performance evaluation, which will happen in November of this year, and biorisk

management improvement, which will happen next month in December. For a list of upcoming ECHO Biosafety sessions and resources from previous sessions, please check out the link at the bottom of this slide. And just for reference, as of October of this year, our ECHO Biosafety web page has had over 6,200 views. Resources for each session have been cumulatively downloaded over 2,700 times. Thus far, we've had 524 unique participants affiliated with 219 unique organizations, located within 50 states and territories in the US. And these folks have been joining the sessions regularly. In addition, the ECHO Biosafety community of practice has reached six other countries, namely Belize, Canada, El Salvador, India, Indonesia, and Italy, with 18 participants from these countries. In addition, individuals from 18 national organizations such as the FDA, the Department of Agriculture, APHL and Pfizer have attended the session as well. Next slide, please.

Laboratories across the country recognize October as Biosafety and Biosecurity Month. Throughout the month, CDC raised awareness of laboratory safety practices across the agency, and with our clinical and public health laboratory partners, reinforcing our commitment to fostering a culture of safety and security. Really, our goal is to strengthen laboratory safety practices and foster a culture of safety and security.

Throughout the month, we highlighted key initiatives and hosted several events. On October 2, we held the first Biosafety and Biosecurity Celebration at Roybal Campus, which is our main headquarters building in Atlanta. It was hosted by the Office of Laboratory Systems and Response. We had over 150 in-person attendees, with over 10,000 personnel having access to join via live stream. The event enhanced awareness and deepen understanding of biosafety security at CDC. On October 9, we hosted a webinar on Safe Handling and Reporting of Highly Pathogenic Microorganisms. On October 16, our OneLab Initiative hosted a webinar on Laboratory Safety in the Age of Artificial intelligence. And on October 22, the ECHO Biosafety Program Session focused on biosecurity aspects of risk management. Collectively, the webinars attracted over 650 participants, including folks from both clinical and public health laboratories, private entities, as well as international organizations. To learn more about our biosafety initiatives, I encourage you to visit our safe labs website through the link on the slide or by scanning the QR code. Next slide, please.

In addition, you may have heard something about viral hemorrhagic fever throughout the news. Our safety team helped review two public-facing CDC guidance documents used by hospitals and clinical laboratories to determine if the existing documents could be expanded to include select viral hemorrhagic fevers, which of course, include filoviruses, arenaviruses, Rift Valley fever virus, Crimean-Congo hemorrhagic fever virus, as well as other high consequence pathogens that require a specialized laboratory, are highly pathogenic and have no vaccine or treatment currently available, such as the Nipah virus disease. Our division determined that all viral species responsible for these selective hemorrhagic fevers are in Risk Group 4 and BSL 4 research facilities are recommended for the propagation of viruses obtained from diagnostic samples or stocks. However, and this is incredibly important, clinical laboratories handling diagnostic specimens from patients must always use standard precautions, including bloodborne pathogens because of the risk of unknown pathogens in any patient specimen. Appendix N, as in Nancy, of the Biosafety in Microbiological and Biomedical Laboratories, or BMBL was created to address the unique risks that clinical laboratories must address to safely handle any patient specimen in order to provide test results for patient care. DLS will continue to collaborate with other divisions to revise external websites to highlight biosafety recommendations for select hemorrhagic fevers. Next slide, please.

Now a few updates on some activities that support diagnostic excellence. Next slide.

Our division, in collaboration with the Agency for Healthcare Research and Quality, or AHRQ and the CDC's Division of Health Quality Promotion, or DHQP, worked to describe the application of diagnostic excellence and stewardship in patient care, hospital, and clinical laboratory settings. This work brought us shared principles and tools for integrating clinical laboratory expertise towards achieving accurate and timely medical diagnoses. An AHRQ-issued brief titled, Diagnostic Stewardship as a Model to Improve the Quality and Safety of Diagnosis was published in August of this year on the AHRQ website. In addition, CDC published the Core Elements of Hospital Diagnostic Excellence, work that was led by our Division of Health Quality and Promotion, in which DLS collaborated as well. And lastly, DLS developed a video called Why Clinical Laboratory Testing Matters, which will serve as a resource for patients to learn about the total testing process. The video uses chronic kidney disease as a model. We plan to release the video by the end of this year and will work with the National Kidney Foundation to disseminate this resource. All of these resources can be found on our CDC website and are available free of charge. Next slide, please.

In addition, you may have heard about the blood culture bottle shortage that occurred earlier this year. And we worked in collaboration with FDA, CMS, and IDSA from July through October. We developed a communication strategy to assist clinical laboratories in handling this expected blood culture bottle shortage. We used our existing channels and networks, as well as our Health Network messages, as well as working with BD on their website to provide information on what to do with this impending blood culture bottle shortage. We provided diagnostic stewardship guidance on how to reduce blood culture contamination, which is something that our division has been working on for a few years now. We also provided

evidence-based strategies to improve inpatient blood culture utilization, given that up to 60% of blood cultures may be unnecessary in practice. Next slide, please.

And now a few updates about our activities that support laboratory readiness and response. Next slide. The Laboratory Response Network for Biological Threats, or LRNB is a coordinated network of public health and other laboratories for which provides standard assays and protocols for testing biological threat agents and emerging infectious diseases. The LRNB was established by the founding partners, which were the CDC, the Federal Bureau of Investigation, and the Association of Public Health Laboratories back in 1999 to strengthen the nation's ability to detect biological threat agents like smallpox and anthrax. In the ensuing 25 years, the LRN has grown substantially and now plays an instrumental role in improving domestic public health infrastructure and increasing laboratory capacity. In the future, LRNB will continue to evolve and adapt to detect new and evolving biological threats rapidly. This ongoing advancement will help ensure that the nation's laboratories remain prepared and resilient, keeping our nation safe. The LRN data exchange works to strengthen the quality and completeness of LRN data so it can be aggregated with external data feeds from other sources, such as those from commercial laboratories or used by CDC programs and year-end responses as well. More information about the LRNB can be found on the website at the bottom of the slide. Next slide, please.

Our division's Clinical Laboratory Engagement team works with both public and private partners on the development of a road map that supports this model of a national response testing framework for enhancing surge testing support during a public health emergency. This work will include a framework, which will be a high level summary of the testing framework and define the scope and public and private partners involved. The roadmap will further explain the partners involved in the response, including when and how to engage with them depending on the public health emergency. The initial scope of the roadmap will be limited to biological incidents of human concern. But future versions will also be expanded to cover both chemical and radiological events. In addition, our division has been updated its memorandum of understanding, or MOU, with relevant testing partners and has increased membership from four originally in 2018, to now 12 partners engaged in discussions for public health emergency response and related to diagnostic testing. Emergency response support has continued this year with supporting the development of an EUA or allowing the continued use of the CDC Non-variable Orthopoxvirus Real-time PCR assay, using high throughput instrumentation within partner commercial laboratories. These efforts have maintained a readiness posture by providing testing capacity greater than 70,000 tests per week from four commercial laboratories and the LRN. Furthermore, DLS has supported emergency response efforts for the influenza H5 response, supporting licensing the CDC H5 test and/or design with commercial laboratories, as well as supporting viral hemorrhagic fever responses, such as the current Marburg disease outbreak in Uganda, with updating laboratory testing guidance for safely and effectively performing routine testing, specimen collection and transport, and proper decontamination when working with suspect patient specimens. The Laboratory Outreach communication System, or LOCS continues to provide up to date testing, emergency response, and information relevant to the broader testing community. The LOCS message system is within the top 10 of CDC subscriber accounts, delivering information to approximately 90,000 subscribers. In addition, the monthly LOCS call provides direct access to both CDC and field subject matter experts for current public health threats that are relevant to the broader laboratory testing community. In the past calendar year, 39 LOCS messages inline, nine LOCS calls have been provided to thousands of laboratory partners to support their testing needs. Next slide, please.

A notable achievement this year was the awarding of a new Indefinite Delivery Indefinite Quantity, or IDIQ contract to external partners to support surge testing, test development, and data sharing. The period of performance of this contract runs from September of this year through 2029. This contract is designed to be pathogen agnostic, and it's an incredible collaboration between the Office of Laboratory Systems and Response and the CDC's Office of Public Health Data. This contract is available to any center at CDC. And it's already used by our National Center for Immunization and Respiratory Diseases, as well as our National Center for Emerging Zoonotic and Infectious Diseases. So it's already making an impact in our nation's readiness and response. The following tasks can be ordered through this contract. First, a warm-based search capacity of 10,000 specimens per week for a limited time. A surge testing of 75,000 to 100,000 tests per week, test development, such as tests for H5 or Oropouche, specimen collection, for example, for migrant farm workers, as well as data sharing for over 200 reportable conditions now can be done through this contract. This is an incredible achievement for CDC and demonstrates our commitment to improving the laboratory system by engaging with external laboratory partners. Next slide.

Just quickly on the Marburg 2024 response, while the outbreak seems to be slowing, the LRN continues to expand testing capacity. We are now at 40 laboratories that can test for Marburg, using a biofire panel that is available only to the Department of Defense and the LRN and select laboratories at the regional special pathogen treatment centers. Next slide.

As shown on this slide, over 8,000 cases of Oropouche have been reported globally, with approximately 20 cases identified in travelers returning to the US. CDC has both a plaque reduction neutralization assay or PRNT and PCR tests to detect Oropouche. However, to enhance our nation's preparedness, CDC is working to develop Oropouche tests and

have them available at commercial laboratories through our IDIQ contract, as I mentioned in the previous slide. And now on to updates on our laboratory training OneLab Initiative activity. Next slide.

DLS developed a OneLab initiative to bridge, train, and sustain a capacity-building community among laboratory professionals and testers, to collectively support rapid, large scale responses to public health emergencies. Several CLIAC recommendations related to the laboratory workforce guided the creation of OneLab. And more recently, recommendations have shaped OneLab's evolution. I'm incredibly happy to announce that OneLab has passed another major milestone. And that is as of October of this year, we have over 41,000 unique members across all of our OneLab elements. In the past two years, membership has increased by about tenfold. We thank our cooperative agreement partners at The American Society for Clinical Laboratory Science, the American Society for Clinical Pathology, the University of Maryland at Baltimore, the Association for Public Health Laboratories and the New York City Department of Health and Mental Hygiene for their outreach efforts, which have contributed to OneLab's growth. This slide highlights some recent metrics for our OneLab resources and members. What I want to highlight one specific metric for the entire fiscal year. During fiscal year '24, we attracted over 439,000 registrations for our OneLab training materials, significantly increasing the fiscal year '23 total of 171,000 registrations, an incredible achievement. Releasing new courses and job aids is essential to OneLab's continued growth. We recently released several new e-learning courses, including one on quality management systems and one on bloodborne pathogens. I'll share updates on upcoming quality e-learning courses in the next section of the presentation. Last week, we released a new autoclave safety practice scenario on OneLab VR or virtual reality. Remember to sign up for OneLab to receive the latest updates. Upcoming priorities include increasing OneLab network participation among CDC laboratory professionals and piloting live, site-specific training on OneLab VR. Next slide, please.

So you have regulations, as you all know, state that doctors of medicine, osteopathy, or podiatric medicine can qualify to direct moderate complexity laboratories by completing 20-plus hours of medical education, commensurate with their laboratory director responsibilities. Currently, several organizations offer training courses intended to meet this requirement. However, none of these courses have been officially approved by CMS. Therefore, CMS has partnered with our division to develop a new, free online CLIA laboratory directory university over the next three years. Guided by the training goal for each section of LDU, our division will design trainings in various formats. Each section will include a pre-test and a post-test that must be passed before the learning can move on to the next training. The program will culminate in a capstone course, where learning learners will apply their knowledge to realistic scenarios they may face in the laboratory. The training materials will have an important additional use as an initial remediation tool for laboratories, cited for CLIA deficiencies. DLS will design an online tool that maps the LDU training materials to common deficiencies, which will hopefully allow CLIA surveyors to quickly and easily assign remedial training based on the specific deficiency for which a laboratory was cited. In addition to measuring knowledge gain and knowledge participation, DLS will also evaluate the Laboratory Director University's short term and long-term impact and revise the program based on CMS feedback. Next slide, please.

Planning for Laboratory Director University kicked off in January of 2024, and CMS has approved the high level training program back in March of this year. Three learning courses will be released in early to mid-2025. Each will first launch as a standalone course on OneLab REACH and later be part of the LDU list of courses. And these are the Introduction to CLIA Proficiency Testing, which will be released by December. The Storyboard for CLIA Personnel Qualifications and Responsibilities. High Complexity Testing has been developed in CLIA. And the course is on track to be released by February. Finally, the Outline for the CLIA Personnel, Qualifications and Responsibilities Moderate Complexity Testing is complete. And the storyboard is in the process of development. The course is scheduled to be released by June. Based on CMS feedback, our division is developing outlines for the remaining trainings and will send them in batches for review. Our goal is to release all 20-plus hours of LDU trainings by 2027, along with the online tool for CLIA surveyors, which will map its training material to the relevant deficiencies. Next slide, please.

And now a few updates on our data science activities. Next slide.

As many of you are aware, Shield was chartered in 2022 as a natural evolution of prior industry and government efforts to achieve interoperability of high quality IVD laboratory test data. To achieve its goals in June of 2023, Shield established a steering committee and in October of that same year created four workgroups who meet on a monthly or bimonthly cadence, a standards and vocabulary workgroup, a litter workgroup, and an IVD datahub workgroup and, lastly, a communications workgroup. Each month, there is an all Shield call where members receive updates from the steering committee and each of the workgroups. Over the last year, the steering committee created a charter for Shield and established a collaborative community. The litter group developed a white paper on the framework for the repository, which will be submitted to the steering committee later this year. The standards and vocabulary workgroup submitted recommendations on updating the laboratory result's interface standard to the steering committee back in September. The communications workgroup developed a member survey that they intend to send to the Shield network later this year. And lastly, the IVD data hub is working to find a contractor who can help create the framework and infrastructure for this resource. CDC has representatives on the steering committee as well as each of the other workgroups to assure that our

agency's goals are represented in Shield's mission. CDC has specifically addressed ways that we can further Shield's initiatives, including hosting our division's quarterly forum on adoption of standards for laboratory data exchange and maintaining the LOINC IVD test code mapping page. Next slide, please.

Our division also continues to work with CMS to improve the automated transfer of laboratory ingrelated data from the CMS iKey system. Using an Application Programming Interface, or API, CMS and CDC have established a data stream with automated weekly pools, where data are accessed, processed with QC checks, and then prepared for integration into the CDC data lake. Currently, we are pulling data from iKeys related to laboratory certification, providers, and specialties. But additional data will soon be included in these data pools. iKey's data along with laboratory-related data from other sources, like provider-level PT data, are uploaded into the CDC data lake. This allows the advantage of gated access to standardized data for CDC analysts. Historical data from as early as the 1990s are being included in the data lake. Studies such as training of laboratory deficiencies and proficiency testing of all this data are underway. Next slide, please.

In addition DLS has a dedicated team of health scientists, data analysts, and a statistician examining the use of real world health care data for opportunities to use clinical laboratory-related information, such as which tests are being ordered and the test result to improve patient care. EHR databases are big data and offer advantages of investigating data from large, diverse populations with rare outcomes, as well as to study long term effects and have been used in studies on treatment effectiveness, safety issues, and cost effectiveness. EHRs can contain US hospital-- excuse me-- based service level information on inpatient discharges, outpatient visits from geographically diverse non-profit, non-governmental, and community and teaching hospitals, as well as health systems from both rural and urban areas. They contain information from millions of patients whose records represent billions of patient encounters. EHRs offer a vast resource of information but are not without challenges. For example, the completeness of laboratory-related data within EHRs due to facility-level laboratory information system integration and comparisons is limited by varying modalities used to measure analytes. As indicated by the asterisk, we've included links to recent publications on this topic. IQVIA and PINC AI are two examples of large EHR databases we have access to and have been exploring for this purpose. I will now describe some example studies that seek to evaluate if recommended genetic screening was done before drug initiation, as well as adherence to best practices. Next slide.

Briefly, DLS participated in a study on screening prior to initiation of abacavir. Please note the abacavir example used IQVIA. And the blood culture contamination used PINC AI. Abacavir is a nucleoside reverse transcriptase inhibitor used as a component of antiretroviral therapy regimens in the treatment of HIV infections. Despite being efficacious and with a few drug-drug interactions, abacavir has been associated with potentially fatal hypersensitivity reactions. Abacavir hypersensitivity reactions have been linked to a specific human leukocyte antigen allele. And studies indicate that the 5% to 8% of the population carrying this allele is at risk of developing the adverse reaction. Despite literature reports, guideline recommended screening, and an FDA Black Box Warning, our study found that only 46% of people prescribed abacavir were screened before drug initiation. While abacavir use is decreasing, there is a broader opportunity to use laboratory-related data to assess the uptake and adherence to guideline recommended practices and to investigate barriers to implementation. These results will be published in the literature in the upcoming months. Next slide, please.

And finally, a few updates on our activities related to health equity in laboratory systems. Next slide, please.

First is advancing Electronic Test Orders and Results, or ETOR, to promote health equity. Of course, we know ETOR enables electronic exchange of text orders and results between public health labs and health care facilities. CDC is helping to establish ETOR between every state public health lab and health care facilities in their jurisdiction by providing technical assistance, enhancing IT infrastructure and funding support. CDC has integrated health equity as part of this initiative and has set a goal to establish ETOR amongst health care facilities that support people who are medically underserved. What have we accomplished? The ETOR initial implementation project focuses specifically on newborn screening to serve as a use case to demonstrate the effectiveness of electronic data exchange. DLS Has collaborated with public health laboratories, health organizations, and laboratory information management system and EMR vendors to design and develop the capabilities and support needed for this initiative in five jurisdictions. It includes Iowa's public health lab and its partner healthcare organization in Alaska, which serves medically underserved areas and populations. We've had several recent successes in Florida, where ETOR went live in August. Partners are already exchanging around 500 orders and results per week, thereby reducing the time to get results into patients' charts by 30% or about two days. The strategies, technologies, and partnerships gained from the initial implementations will be used to expand ETOR to other use cases and to other partners that include health care providers in medically underserved areas and populations. Next slide, please.

Another project that we have been involved with includes an LDL lab messaging project in collaboration with the Million Hearts Initiative. We have described this project in previous CLIAC meetings. And it is designed to achieve a timely diagnosis of severe hypercholesterolemia and statin prescribing to reduce risk for heart disease and medically underserved populations. Of course, underdiagnosis and undertreatment of severe hypercholesterolemia is established as a gap in US health care, with over 80% of persons undiagnosed and undertreated. Additional data analysis are

currently under way from the initial pilot to confirm the findings, which indicate positive results through the use of lab messaging to physicians. Specifically, this process was implemented at Zufall Health, which is a federally qualified health center in the State of New Jersey. And at the next CLIAC meeting, we should have an update with the figures that we need to confirm that have been received from the implementation of this project. But it's incredibly promising, the outcome of this particular project. Next slide, please.

Now, since launching in 2022, the career pathways in public health laboratory science program has placed over 420 fellows and interns in state, local, and territorial laboratories across the United States. This program is a collaboration between our division and the Association for Public Health Laboratories. Our health equity goal here is to increase the percentage of fellows and interns from underrepresented groups and communities by 40% by the year 2026. Career pathways applicants complete an anonymous questionnaire that captures demographic variables, which include race, ethnicity, gender, age, sexual orientation, disability status, and pre-college socioeconomic status. Fellows and interns complete the anonymous survey again once they enter the program. After gathering baseline data, we are now working to prioritize the list of demographic variables to refine our implementation plan with input from a cohort of subject matter experts in laboratory education and diversity, equity, inclusion, and accessibility. These SMEs are also compiling feasible and actionable ideas. To accelerate our progress toward meeting this health equity goal, DLS and APHL will use these insights to inform an updated implementation plan next summer. Next slide, please.

And that was a lot. And there will be a quiz in a few minutes. I want to thank you all for your attention. Thank you for providing me the opportunity to share all of these successes with all of you and to once again remark on the importance of the laboratory system in the United States. Thank you. Back to you, Jordan.

CLIAC CHAIR: Excellent. Thank you so much for that update. We're a little bit behind schedule. So I'm going to say let's reserve questions until the end. Why don't we just roll on to the next update from CMS? Gregg, take it away.

Centers for Medicare & Medicaid Services (CMS) Update
Gregg S. Brandush, RN, JD, CMS Ex Officio

MR. GREGG BRANDUSH: Thank you, Jordan and Laing, for first presentation and CLIAC knocked it out of the park. That was outstanding. So my name is Gregg Brandush. I'm the director of the Division of Clinical Laboratory Improvement and Quality, or DCLIQ. Throughout this presentation, I'll also be referring to us as CMS CLIA just to add confusion to the presentation.

First slide then, this is a standard disclaimer. First time I did this, I read this verbatim, word for word. I'm not going to go through that again. The main takeaway here is that this is for informational purposes. It should not be relied upon as official guidance. And any errors in this presentation are mine. There's also nothing really substantial in this or substantive in this. So I don't think anybody is going to run the risk of acting on anything here anyway.

Our organization-- so when we presented last April, we had just gone under reorganization. It was hours old. And we're still trying to figure everything out. We've had a good six months now, more than six months, to try to figure things out. And things are in the process of settling in. There's still some communication issues that we're trying to work out. But this is the broad structure. So there's me, the director. There are five technical advisors. Elysse Lessner is the enforcement technical advisor, Scott Stacey for our data, Karen Sutterer for survey, Penny Keller for regulations and clearance and Cheryl Dobie for state oversight. We are aligned along five branches that reflect the primary product line of the agency. So we've got a survey branch led by Dan Hesselgesser, an enforcement branch led by Latoya Laing, a logistics branch led by Karen Fuller. And that's the one that probably is most not immediately obvious what the logistics branch is. And the logistics branch is the catchall that grabs all the stuff that doesn't fall neatly in one of the other branches. They handle data. They handle our budgets. They handle FOIA requests and that type of thing. Regulations and clearance is led by Angie Daubert. And then the state oversight branch is led by Raelene Perfetto. One of the things that was a major priority when I came into this role three years ago was to stabilize the CMS leadership team. There had been a lot of turnover in the years previous. I'm really happy to report that our team remains the same from last April. And the only changes from the presentation a year ago is some of our technical advisors have been assigned to the positions permanently. So we've been able to bring stability to leadership, which is really important to move any program forward.

So the number of labs, how many labs there are-- this is always an interesting slide. So you can see right now the number is 314,000 roughly. If you have an extraordinary memory, you'll recall the last time I presented this, it was about 317,000. There's a couple of reasons for the decline. Historically, we've counted on pretty much a 2% growth in the lab community year after year. As you know, during the public health emergency, there were a lot of labs that sought certificate to provide COVID testing. We are seeing those labs decide that they were just in it for COVID, and they don't want to continue being a lab. The number that's most telling for that is the certificate of waiver number. So we see there's roughly 255,000 certificate of waiver labs right now. Last time I did this, that number was 257,000. So a good 2/3 of the decline is from that laboratory setting. Certificate of compliance and certificate of accreditation are roughly the same as is the exempt states

and PPM. The other difference is just the way we are collecting this data. So during the public health emergency, one of the flexibilities we offered was to allow a laboratory to begin testing as soon as they submitted their application. It was really important at the time because feed-in testing was the priority. That's what we wanted to push. What we found is many of those labs never paid because under the normal circumstances, a lab has to pay their fee, and then they can begin testing. We're no longer in a public health emergency. So we've gone back to our traditional approach requiring a lab to pay before they can begin testing. And that is further contributed to this overall decline. Maybe next time there'll be a slight decline as well. But I'm hopeful we'll see progression in our numbers going forward.

So this was the slide that I presented last year or last April. And during that presentation, everything that was highlighted were things that we accomplished. And there are a couple of things here that are evergreen. So improved processes are evergreen. Modernizing the CLIA program is evergreen. And the engagement is evergreen. The adherence to enforcement timelines is something we didn't quite achieve. So one of the things I wanted to share is that when we have these goals-- and if we don't make them, it's not like we go shucks and move on. Latoya Laing, the branch manager of the enforcement branch, has done an amazing job leading efforts along these lines and with the assistance of her entire team and Elysse Lessner, the technical advisor. So I want to go over what they've been able to accomplish in terms of enforcement because I think it's really impressive.

So these are enforcement frames for our reorganization, so roughly March of I think last year, 2024. But regardless, March 2024, we had 97 cases. The number of days before it reached us was an average of 50 days. So the state agencies, they identify condition level non-compliance. They work with the lab to try to return to compliance. If they're unable to do so, they refer it to us for enforcement. And you may look at this and say, OK, well, what's the big issue? One of the concerns is there's a regulatory requirement for us to impose a suspension of Medicare, Medicaid payment if there is a condition level non-compliance for 60 days or more. It doesn't give us much time to act on it and definitely doesn't give us sufficient time with notice requirements. In the enforcement process, there is a notice expectation where we propose a sanction, give the laboratory the opportunity to respond to it, and then impose it later. So the average time to propose a sanction is 120 days. So you could see that as well above that 60-day period that we're looking for.
And the average imposition was 128 days. The average total enforcement days is 138. The reason that number is concerning is we had more than a third of a year. That's a laboratory that has serious non-compliance. We want that shut-- we want that lowered significantly.

So let's look at what Latoya was able to do. So this is a shorter period. So this is through September 30, 2024. There are 30 cases we looked at. The average pre-enforcement day was 24.89, proposed day, 22.1, imposed, 57.58, and total enforcement days, 66.29.

So looking at a comparison there, what that looks like-- she reduced the pre-enforcement days by more than 50%, which is fantastic. The average proposed has been reduced by 81%, which I think almost is not possible. Average imposed reduced by 55%. And the total enforcement day was a reduction of 52%. That reflects a really remarkable step forward in ensuring quality. So to reduce the time that there is testing that we can't be assured is accurate and reliable by 50% is pretty extraordinary. So I just wanted to give a shout out to the enforcement team for this accomplishment. I'm really proud of it.

So these are some of our goals for 2024 and beyond. This will be updated in April with new goals. So in 2024, what we wanted to accomplish is to ensure that 50% of the CLIA certificates will be electronic and available online. We've got that. And I will say about this electronic certificate, it's great to have it on QCOR. Anybody could see their certificate there. But just having a certificate that's available electronic, online. That's good. That's great. But that isn't really the goal. Really the goal is to be a fully electronic process. So that's something I'm going to address a little bit later. But we do have this specific goal. 50% of them are online, which is outstanding. We intend by the end of this year, calendar year, to issue the new interpretive guidance on the new fee, histocompatibility personnel, and alternative sanction rule. So that will be highlighted out next time. We addressed some really significant inconsistencies related to survey team size, time spent on surveys citation rate especially with respect to APHL labs. In a future presentation, I'm going to share that data because Dan Hesselgesser has worked really hard along with Karen Sutterer to bring that into line. We see the tracking enforcement actions. We went over that. And the last goal there for this year to make the CLIA certificate of compliance surveys available on Q shore. This has been a little more challenging than we expected into making sure that there's automated redaction programs in place, in case there happens to be PHI, PII included on a survey finding. This may have to be kicked to year three or later. We're going to have to take a look at that. But this is really born-- when I gave a presentation to the accrediting organization, they were really concerned about this and wanted to know why we were doing it. And it is to further goal of transparency primarily. And a second reason is the number one request we have when we get FOIA requests is people want to see the 2567. They want to see the survey report for a lab when there's a concern. And there is an obligation under FOIA that if an agency knows that a particular type of information is commonly requested and it's going to be commonly requested that we proactively make it available. Year three goals, I won't go into this too deeply because Victor did an outstanding job. But Lab Director University is one of the things, again, I'm really proud of. Our work with CDC on this is pretty extraordinary. Cheryl Dobie is leading the effort from the CMS side. And

that's going to be a really powerful tool when that is up and implemented. And then more long term, we're going to revise our enforcement letters because they're written very lawyerly right now. And they're very difficult to read and understand and are complicated. So plain language those. And then look at our budget allocations to make sure that they are fair and standardized. And the year five-- again, that's expanding the Lab Director University effort to other areas and then looking at our survey process overall to make sure that it's subjective, consistent and hopefully computer assisted.

Some additional accomplishments, in conjunction with CDC, evaluated all the proficiency testing providers to ensure they're ready to go with the new PT regs and are going to hit the ground running in January 2025. I mentioned during the electronic certificate item that our larger goal is really to be fully electronic. So we are fully electronic with 35% of labs, which is really excellent. But we need to get further. We need to get 100%. So we have a plan in place to convert to a fully electronic process by 2026. Victor mentioned the BD BACTEC blood culture vial issue, which we had a lesser role in that because the CLIA requirements didn't change that much. But we were participants in that effort-- provided an additional certification for cytotechnologist, eliminated survey backlogs in eight states. So this is really understating the accomplishment because when I put this presentation together, I think I didn't realize the scope of the accomplishment. So during the public health emergency, there were survey backlogs that resulted-- surveyors were unable to survey for a variety of reasons. Some states diverted them to other more pressing public health emergency issues. People had personal health concerns. There was PPE shortages. There are a variety of reasons that resulted in survey backlogs. So when we were looking at states efforts to eliminate these backlogs, they were trained to survey their way out of it. And if a state has a backlog of just one survey, so going back two years, and they start surveying every year to catch up with that backlog, it would take four years just to get caught up. And it would then also quadruple the cost to the program. And when we were looking at that approach, we didn't see a lot of value in it. Because when a surveyor comes into a lab-- and even if there was a backlog of a survey or two, they are establishing compliance with all the CLIA regulations current. So we know when they leave the facility or when corrections are made, that that lab is current. So we didn't see the value and actually saw it as a really inefficient use of program resources to do back surveys. We moved their certification up so that they're compliant going forward. That was one aspect of it. Another aspect was the states that their concerted efforts to eliminate backlogs and get caught up-- we had federal surveyors that went out and volunteered to help states that either had backlogs. Or they had surveyors that were unavailable for a variety of reasons to ensure that they maintained the current status with their survey workload. And all in all, over the course of six months, this eliminated the backlog by 33%, which is really significant. And then additionally, we have databases to monitor our communications with the state agencies. And then we've improved or increased our reengage. That's the word I'm looking for. We re-engaged our regular communication with the accrediting organizations and exempt states.

New policy memos. There was only one. And it was really a technical correction. Some analytes weren't categorized under endocrinology. And one of the units was incorrect in the Federal Register. We published a correction in the Federal Register to correct that. And then we published a memo just to give everyone notice that these corrections were made. It was really a minor memo. There were two new administrative memos. And these are pretty standard. We do these pretty regularly. The SAFER is something that we do every year. The budget call letter is something we do every year. And then we had some administrative revisions to how we're looking at plan to corrections and allegations of compliance and then had the memo about the new board certification for cytology. But with that, I think that's it. We're still a little bit over. But I went through that little quick to get us back on track.

CLIAC CHAIR: Thank you for the update. The updates have been fantastic so far this morning, just a ton of information shared. So really appreciate it that still holds questions for the end. And we could roll right through to the FDA update. Courtney?

Food and Drug Administration (FDA) Update
Courtney H. Lias, PhD, FDA Ex Officio

DR. COURTNEY LIAS: Thank you, Jordan. I'm Courtney Lias, again, director of office of in vitro diagnostics at FDA. And I have a few updates since last April. So next slide, please.

First, just to remind you here at FDA in our office, we regulate the full spectrum of in vitro diagnostic tests. And that includes pre-market regulation. So when companies are developing new types of tests or new tests of similar types, they come to us to get pre-market authorization. And then once they're on the market, we have requirements and work with companies to make sure that those tests stay safe and effective for use in your laboratories. We provide guidance. And of course, you're familiar with some of our activities when there is a 564 emergency. So next slide, please.

One of our key areas right now really is home use testing. And it's an area that's been around for a while but has gotten a lot more attention since the COVID pandemic. Given the usefulness of having COVID tests at home to help people make decisions about their activities, health, and family. And some of the advantages of expanding the availability of home use tests of various types is that they really do help in a lot of ways people to have additional privacy or access to tests that they might want. They may not have to wait for an appointment with their physician. They may be able to transition sooner

from a health care environment back home in some cases. And they might be able to help mitigate the spread of some conditions if they're able to get access to testing that they might not otherwise have access to. Next slide.

When we are assessing whether or not something is appropriate for home use-- and that would include home use with a prescription or home use without a prescription. There's a lot of things we think about. And this slide shows a subset of those things, certainly not everything. One of the important things is specimen type. So we really do consider how easy would it be for somebody at home to get a specimen. A very common specimen type at home is urine, for example. It's very easy for a home user to collect a urine specimen. An additional home user type might be capillary blood with spring loaded lancets and home capillary blood collection devices. But it would be harder to collect venous blood at home at the moment. And there's some types of specimens where it might be more simple for someone to collect a nasal swab. It is a little bit more challenging to collect a nasopharyngeal swab or throat swabs. And so really the design of the collection devices and the design of the test itself matters a lot when you're putting a test over the counter or for use without the assistance of a trained laboratory professional. We also consider the complexity of actually running the test. So many of these you'll see are similar to pregnancy tests, which have been around for a long time, where it's a lateral flow immunoassay that's relatively simple to use. But there's other models as well that might be designed in a more complex manner. But hopefully running it is very simple for the person using it. And we also consider the design of the product itself. You certainly wouldn't want a product that had toxic reagents, especially if people have young children running around or if they may not have personal protective equipment to use while running that test. And then finally, the labeling and the instructions and making sure people understand both which tests to select and when to select them and how to use and interpret the test is really important. So the instructions-- making sure people understand them and don't misuse them is really important. We have a lot of stories about consumers who misinterpret how to use home use tests, for example, putting them in the microwave to disinfect them or using specimen types in a way that isn't intended. And so critical evaluation of how people might interpret your instructions is always important. Next slide, please.

Even given all this stuff, we have a really long history of having home use and home access tests. And in the last 10 years, we have authorized over 400 of them and many more even before that. So lots of them have been around for a while, including pregnancy tests and blood glucose tests. But each year we're getting more and more. And I think you all realize this. But one of the areas that's fastest growth in the home use environment is infectious disease with a real desire to provide more and private access to infectious disease testing for Americans. And so we're really working hard on that. Next slide.

In April, I updated you all on an announcement we made earlier this year related to how we might optimize the regulatory pathway for certain types of IVDs that come to us. And so we announced that we plan to reclassify, with respect to FDA regulation, most of our high-risk tests. And what this means is these tests are still high risk. But we've learned enough about them. And what types of things can be done to mitigate those risks to acceptable levels such that we can put a lower regulatory burden on those tests? And so we do what's called down classify. That requires rulemaking, which means making or changing a regulation. And so the process can be relatively long. But since April, we do have some encouraging updates. On September 25, 2024, we were able to put out a proposed regulation, meaning we are proposing to downclassify tests for hepatitis B. And this would include antigen, antibody, and nucleic acid base tests for hepatitis B. And there is a comment period for that proposed rule that ends in November 25. So if you have any comments on that, please submit those to the docket. We'd be very interested. And then on October 23, 2024, we issued the final order, so the actual downclassification of CMV assays for transplant patient management. And so those assays are no longer in our highest category called pre-market approval. Now what's called 510(k) or pre-market notification pathway can be used for CMV tests. And we have additional reclassifications in the works, including our intent to reclassify companion diagnostic tests. So we'll continue to keep you updated on the progress for this. Next slide, please.

I know you've heard some about this. But we continue to work very closely with the CDC, with NIH, especially the ITAP program, with CMS, and BARDA and others on the response for the highly pathogenic avian influenza. And a lot of our efforts in this area have been assessing current flu A tests to find out whether or not they would be helpful in the response efforts. And luckily, most marketed flu A tests are expected to detect this avian influenza strain with a positive result. And so I wanted to highlight today that we have a website that lists our influenza A diagnostics that are available as a helpful resource for people who are looking for flu A tests. And we'll continue to keep you updated as we get information that may help in this type of response. Next slide, please.

In addition, we continue to work on COVID and impacts, two of our areas that do have 564 emergency use declarations. I mentioned last time that we are encouraging people who have emergency use authorization for COVID tests to transition those into traditional marketing pathways. The advantage of this is that your test can then be available with a lot more certainty for longer, for example, if the public health emergency were to end. And we have already transitioned into traditional pathways on a lot of tests. So we encourage you, if you have one of those, to reach out if you're not sure how you could do that. And for impacts, we continue to work very closely with CDC and others to make sure that tests are adequately available across the country for old and new strains alike. Next slide, please.

Sometimes we have cases where tests are on the market that are no longer suitable for use. Last May, we put out a safety alert related to Cue's COVID-19 tests because of some modifications that resulted in an increased risk of false results. Since then, Cue Health has removed those tests from the market. And they are no longer available. And in October, we actually revoked the emergency use authorization for those tests. And they have been recalled. So this is an example of a case where a test may be working. But when it stops working, we really do work with the company to try to mitigate the risks to patients. Next slide.

One really exciting effort that culminated in June of this year is the effort to put out a point of care molecular test for HCV as a really huge step in the test to treat program toward the reduction or elimination of HCV in the United States. And so through the ITAP program, Cepheid's Xpert HPV test was authorized after basically starting the studies in January. It was authorized by the end of June. So it was an extremely efficient teamwork between CDC, NIH, FDA, Emory and others to make sure that we could get the information we needed to put this really important test out there. And the impact, as you all know, is that patients, including underserved populations that may have been difficult to treat before now can get tested, get the results, and potentially start treatment during the same doctor's visit. So we're really excited about the potential that this tool can provide in this area. Next slide, please.

In the home use area, we have a couple of announcements as well. In August, we authorized the first over-the-counter syphilis test. So this is a capillary whole blood test used at home in 15 minutes to get an initial result for syphilis as a way to help people make decisions about how to interact with the health care providers. It's certainly not a replacement for interactions with health care providers. But it is another tool to try to increase testing in an area where people may be hesitant to test. So really, congrats to the teams that made that happen. Next slide, please.

We also expanded the indication for Insulet's SmartAdjust technology for diabetes. So previously, automated insulin dosing systems, sometimes previously referred to as artificial pancreas but now called AID systems, automatically adjust insulin and deliver insulin based on continuous glucose monitor readings and have been solely available in patients with type 1 diabetes. But with this authorization, the Insulet SmartAdjust technology AID system is available for millions of people in the United States with type 2 diabetes, who rely on insulin. It's a really exciting development because these AID systems have really been shown to improve glycemic control in people and to maybe, more importantly, really significantly improve their quality of life. So we're really excited to see the impact that this and other developing technologies may have. Next slide.

In the home use area, again, we in October authorized Healgen's combo flu A/flu B and COVID 19 home-use over-the-counter test through our traditional marketing pathway. And so while we had had similar combination tests for flu and COVID out under emergency use authorization, this represents the first traditional pathway market authorization and will create a pathway for other of the emergency authorized combination tests to reach the market more permanently through this traditional marketing pathway. So this was a great partnership as well with the ITAP program that performed the validation for this Healgen authorization. Next slide, please.

And finally, got through this very quickly, it's been a year for colorectal cancer screening tests. So we actually had three approvals in the colorectal cancer screening arena that I wanted to highlight. The first is Geneoscopy ColoSense test, which was approved in May. This is an RNA-FIT plus occult hemoglobin test meant to screen for colorectal cancer. The second, in July, we approved the Guardant Shield, which is the first cell-free DNA blood-based screening test approved, which can provide alternatives especially for average risk individuals. And then finally, Exact Sciences has updated their Cologuard test to the Cologuard Plus. And that was approved a few weeks ago and will soon be available. And these types of screening tests are meant for people at average risk of colorectal cancer and can provide options to people who may otherwise not get screened. And so there's really a lot of hope in this area that we will reach a lot more people. Next slide please.

I went through this very, very quickly. I am happy now or later to take questions from the panel. But anyone who has questions for us, here are some ways to find information. And please don't hesitate to reach out. And with that, I'll close. And I really look forward to the discussion later. Thank you.

CLIAC CHAIR: Again, thank you all for all the updates. They were probably the largest amount of updates we've had at a CLIAC meeting that I recall. So we do have five minutes. So I'll open it up to the committee to see if there's any questions for any of the speakers that provided the updates. And we can finish this off before we break for lunch. Any questions from the committee? [CLIAC MEMBER], I see you raised your hand first.

CLIAC MEMBER: Yes. Thanks, everyone, for providing these updates. I have a few questions. I wanted to start maybe with Victor. I think when you presented the information on the various emerging pathogen, that was really cool. I'm curious, how do we determine-- how does the CDC determine which one to focus on? So, for example, this summer EEE virus was raging a little bit in New England. But I didn't see any discussion of EEE. So how do we decide when or what organisms to focus and try to get diagnostic going for?

CDC EX OFFICIO: I will say that, of course, CDC has its Office of Readiness and Response as well as our emergency operations center and other activities throughout the agency. I admit to not knowing the exact process by which pathogens are closely followed. So I can certainly follow up on that process to send it to both you and the rest of the committee to answer that question because I am not intimately familiar with that process. I do get to see the reports. And, of course, we're involved within the graduated response framework that we now have at CDC.

CLIAC MEMBER: Very cool. Thank you. The other question I had for you was related to the lab director university. Is that what it's called?

CDC EX OFFICIO: Yes.

CLIAC MEMBER: So is this for individuals that don't have a board certification that they need to be trained on being CLIA director? I'm trying to understand how that's different from a board-certified pathologist or microbiologist that's learned this to the fellowship program, for example. So is this targeted to a specific group of MDs or the list that you had on that slide?

CDC EX OFFICIO: Actually, I will defer to [CMS EX OFFICIO] on this question.

CMS EX OFFICIO: So under our new personnel requirements, there's a regulatory requirement for any laboratory director of a high complexity or moderate complexity laboratory. They have to obtain 20 continuing education units. There are a variety of sources for these units. But they're all things that people have to pay for. And so what we wanted to do because we have this regulatory requirement-- we want to create-- of course, that's freely available to laboratory directors-- is really specific, specifically geared towards achieving compliance with regulations. And it's going to address one of our long-term secondary goals where we've got the top 10 deficiencies. I've done that in the past where they're the same year in and year out. And then a third prong of this is if we have a lab that has condition level non-compliance, Latoya and her group can use that as an enforcement remedy. We could say because of this noncompliance, you must take this course so that we know they've got the training to address the non-compliance.

CLIAC MEMBER: There you go. Thanks, [CMS EX OFFICIO]. [CLIAC CHAIR], do I have time still or I have to shut up now?

CLIAC CHAIR: If it's all right, let me-- I see [CLIAC MEMBER] has a question. We have time for one more, so I apologize. Let's let [CLIAC MEMBER] have the floor. Go ahead.

CLIAC MEMBER: Quick question. With all of these point of care influenza assay, for example, I'm recalling how the EIA assays had to be retested every year to make sure that they were detecting the various strains of influenza being spread through the communities. Will that apply also to these point of care tests that people are doing at home? Thank you.

FDA EX OFFICIO*:* Yes. All the flu A tests will be assessed in the same manner, including the over-the-counter ones. Thank you.

CLIAC CHAIR: And, well, with that, we are right on time. So thank you all very, very much. We'll now take a one hour lunch break. I guess if you're on the West Coast, it's probably more appropriate to call it a brunch break. And we will return at 1:50 Eastern time. I believe that's 10:50 Pacific time. And we'll begin our CLIA workgroup report sessions. Thank you very much and enjoy some food.

❖ Presentations and Committee Discussion

CLIAC Workgroup Reports

The Biosafety Workgroup
Michael A. Pentella, PhD

CLIAC CHAIR: Wonderful. Well, I hope everyone had a good lunch or brunch. And we'll move on to our first topic for the day, which is-- the remainder of the day, we're basically going to have to CLIAC workgroup report outs. We're going to start with the biosafety workgroup report, which is going be presented by the workgroup chair, Dr. Michael Pentella. And this will be presentation 5 and report 5a that's on the CLIAC website. So as always, after the presentations, we'll have some time for public comment, followed by a committee discussion. And so with that, it's my honor to turn it over to Michael to take us off.

DR. MICHAEL PENTELLA: Thank you, Jordan. I'm going to share my screen and then share this presentation. Go into presentation mode. Hey, are you seeing it in presentation mode? Or should I swap to the present—

CLIAC CHAIR: Yeah. You probably should swap. We see the presenter mode.

DR. MICHAEL PENTELLA: There we go. Thank you very much. So to present today, first I want to remind the attendees that CLIAC has issued five recommendations to address biosafety, dating back to 2001, the most recent being in November of 2019. And those can all be found at that link.

Just some quick definitions-- we're defining the operator and the laboratory director here as the person who meets the stated criteria. And then, there's a standard for the facilities that's listed there. And there's also subpart R enforcement procedures at standard 93.1804.

Those all are important for considerations in this report. So the workgroup charge was provided to us to provide input to CLIAC for consideration in making recommendations to the Department of Health and Human Services on the potential additions to CLIA regulations and the need for solutions that will provide a safe working environment for the nation's clinical and public health laboratories.

So to achieve that charge, we put together this workgroup members. And some of the members you'll note are members currently of CLIAC. And others are past members of CLIAC as well and volunteers from the community with expertise in this area. And so I won't list each name. But they were a great group of people to work with, very engaged. And we had excellent conversations around the questions that I'm going to tell you about.

So I'm going to start with question one. And we looked at in-vitro diagnostic test instruments and looked at the design and how it plays a key role in mitigating biosafety issues that arise during the routine use and maintenance schedules. So we wanted to know how can interested parties better address biosafety for already established instruments and instruments currently under development. So we started with question 1A, what mechanisms, best practices do manufacturers currently use to assess biosafety considerations? And are there current mechanisms where end users can discuss or highlight biosafety issues with the established instruments in the communities? And are there mechanisms currently in place that can be developed that would facilitate collaboration between manufacturers and variety of clinical lab representatives?

And we went on to discuss in designing new instruments, what biosafety considerations are there? And we wanted to consider what considerations are typically given to biosafety with respect to the design. What's considered for the robustness of instrument parts, the material to routinely decontaminate the instrument with, sterilization procedures, use of disposable parts in the areas of the instrument that can be changed out. And also considered, are there mechanisms in place that can be developed that would facilitate collaboration between the manufacturer and the clinical lab community during the design phase so that new instruments could be developed with improved biosafety features in mind?

So for question one, our discussion points and consistent consensus are listed here. There's a consensus reached that laboratories should have a requirement to perform a risk assessment on all instrumentation currently in use and before purchasing new equipment. The second is laboratory equipment manufacturers do have protocols for disinfection and/or decontamination. But they are mainly from the standpoint of the instrument itself to avoid or prevent cross contamination for the specific agent that you're trying to detect so that you don't get a false positive. It was emphasized that often these instructions are not clear. Or they may be hard to locate in the operating manuals. And they're focused, again, on the patient versus the laboratorian who's operating the instrument. So we discuss that there are robust model systems and appropriate assays that need to be created to generate biologically meaningful decontamination data that can be extrapolated to an emerging pathogen because as we know, many emerging pathogens have been seen in the last few decades. And the last point on this slide, instrument cleaning and decontamination guidance should be standardized and easily identified in the instruction manual that's provided to the end user. You need a central location, repository or website that manufacturers can use to post the guidance. And that would be very helpful for everyone involved. So that was our consensus in discussion involving question one.

We moved on to question two. And we note, in these questions, laboratories receive and handle specimens that contain unknown pathogens. Everything that enters a clinical or public health lab, for the most part, is an unknown pathogen and routine basis. How can interested parties ensure proper biosafety activities for end users are established, effectively provided, and communicated and followed by the end users? And are there widely-available training materials for laboratory professionals that focus on instrument operation and cleaning and disinfection practices? Do currently available biosafety training materials include sufficient information regarding instrument disinfection? If not, what minimum information should be included in these trainings? And are there mechanisms in place that can be developed by laboratories that would ensure annual biosafety training and/or competency assessment of the laboratory staff?

So we took these questions to the workgroup. And the workgroup discussed informed consensus. Consensus was reached that there is inadequate biosafety training related to instrument operation and decontamination. Training should be developed to include the service engineer, the application specialist, the trainers and others who are not necessarily medical technology trained. And it's the laboratory director who's responsible for ensuring that individuals entering that laboratory are trained in disinfection and decontamination cleaning procedures, especially maintenance procedures. So the next consensus point was partnerships with manufacturers are essential in developing training for new instruments. And the third point is training should be provided for the entire laboratory process with people from different perspectives. So you have to include different parts of the laboratory, chemistry, biology, microbiology, then also surgical pathology and other different sections of all of the laboratories. Ideally, the training will include case studies and provide the learner with more basic understanding of where the dangers come from and how to identify hazards, so they can do a risk assessment on their own, and how to start mitigation procedures. So it was acknowledged that no standardized mechanisms are in place to assess biosafety competency adequately for laboratory staff. And these should be developed. So those were our consensus for question 2. There's four questions.

Moving on to question 3, what additions to the CLIA regulations could be made to ensure that laboratories are required to have policies and procedures addressing laboratory biosafety? So we cite here the current facility standard 493.1101. And part D indicates that safety procedures must be established, accessible, and observed to ensure protection from physical, chemical, biochemical and electrical hazards and biohazardous materials. So we ask, should the CLIA regulations be updated to include additional safety standards as related to facilities that could include but not be limited to-- these items are listed below-- The proper workspace and ventilation to safely handle contaminated specimens for pathogens. Pathogenic organisms at the appropriate biosafety level. Proper decontamination processes in place to help minimize contamination. Appropriate biosafety equipment and personal protective equipment available in accordance with appropriate biosafety levels. And lastly, a requirement to report results of highly infectious organisms, potential agents of bioterrorism, and unusual multidrug-resistant organisms to state public health laboratories or CDC, as required by the federal government's state or local government authority.

And then there is a part 3B to this question. Should CLIA regulations be updated to include additional safety standards related to general considerations?

And we had discussion around question 3 and reached some consensus. We feel that revising CLIA's guidelines might have cost implications for laboratories and should be based on the risk assessment process that each individual laboratory performs to address their site-specific needs for each laboratory category. We further recognized and reaffirmed that the FDA review process for new instrumentation does not include biosafety aspects but is more in the context of potential cross contamination prevention or cross carriage of samples themselves to determine if there's a potential for a false positive or negative result. It was agreed that the manufacturers should refine and provide the scope of decontamination of laboratory equipment through the risk assessment process that they would do and provide this information to the purchaser, the end user of the instrument. Defining the range of the risk assessment was emphasized. It was agreed that the language should be comprehensive, including hazard assessment, mitigation, and performance monitoring so a more specific definition of risk assessment be made available to clinical laboratories. And lastly, an agreement was reached that reporting requirements for the identification of certain pathogens should be kept general but noted that better synthesis and coordination are needed from the agencies on reporting requirements.
So that ended our discussion of question 3.

Our last question, question 4, we asked-- clear instructions and communication are key to addressing biosafety. Therefore, how can manufacturers and clinical laboratories work together to provide clear, readily available biosafety instructions for each phase of testing, for cleaning and disinfection practices and maintenance of the instrument? What resources are available for manufacturers to gain biosafety-related input to develop appropriate instructions? We have the EPA lists, OSHA regulations. And how can manufacturers gain input from biosafety professionals to aid in the development of supplemental biosafety testing instructions for end users and service representatives? And lastly, how can non-regulatory organizations like the CLSI and others, professional societies, help in this process for manufacturers and laboratories.

So we had discussion and consensus around these questions. We concur that increased collaboration between equipment manufacturers and clinical and public health laboratories need to be encouraged. It was suggested that organizational approach between the interested parties would be more appropriate for developing these resources. The workgroup suggested that FDA explore adding a requirement that the manufacturer provide biosafety guidance as part of the product review and clearance. A common theme was the notion that a space should be created to serve as a centralized repository for biosafety information that both the manufacturers and end users can access. And the workgroup discussed updating CLIA requirements to include biosafety training as part of testing personnel competency requirements, so part of the annual competency assessment. It requested the development of an implementation guide for the competencies that already exist that are out there. It was clarified and reinforced that the manufacturer's instructions for

use must be sufficient for users and manufacturers service personnel to accomplish disinfection and provide sufficient detail to allow incorporation into the laboratory's site-specific risk assessment.

So now I'll end with providing what the workgroup agreements are. So as a workgroup, we agree that a standardized definition for biosafety risk assessment should be developed and added to the standard. We agreed that language in the definition of the biosafety risk assessment should be comprehensive about the risk assessment, including the hazard assessment, the mitigation, the management, and the performance monitoring. Also agreed was that laboratories should be required to perform a risk assessment on all instrumentation currently in use and before implementation of a new instrument laboratory should consider biosafety risk when purchasing new equipment and must complete a risk assessment before you purchase the equipment. And the workgroup agreed that the standards should be expanded to clarify that laboratory workers and, in turn, the general population should be safeguarded and right now refers specifically to the general population. And the workgroup agreed that the FDA requirement on biosafety risk assessment for device approval would support clinical laboratory biosafety and the health of the public.

We went on to further agree that it's the laboratory's responsibility to obtain the written equipment disinfection instructions and practices, preferably before purchase so that you could review it for your risk assessment. Additionally, end users should incorporate the manufacturer's detail, instructions, and practices into their biosafety risk assessments and routine practices. Further agreed was that clear requirement should be revised to include biosafety training as part of testing personnel competency requirements. And we agree that there is a need for annual biosafety competency assessments. And we agree that there is value in increased collaboration between the equipment, manufacturers, the clinical labs and public health labs and regulatory agencies to improve knowledge of instrument risks and hazards and effective mitigation and decontamination practices. We need additional research to determine the best path forward. So those are our nine agreements that followed the four questions that we discussed. And we're ready for questions and further discussion.

Public Comments

CLIAC CHAIR: Excellent. Thank you for the presentation. Before we go to committee discussion, I know we have time for public comments if any. Heather, do we have any?

CLIAC DFO: We have not received any public comments on this topic.

Committee Discussion

CLIAC CHAIR: So we could roll right into the committee discussion. And what I'll share to kick us off-- so what's one of the lovely things about the workgroups as the output of these are agreements-- so the agreements are the committees cheat code. So we have the ability to accept the agreements whole-- accept the agreements as they are. But also, of course, we have the opportunity to deliberate and pick things apart if we would like to. So I would say for efficiency's sake, let's discuss any of the agreements that we want to discuss a little bit more deeply or refine. And certainly, the ones that we agree with we can just let pass through. So I'll open it up to the committee to begin asking any questions or provide any comments.

DR. MICHAEL PENTELLA: Would you like me to put the agreements back on the screen, [CLIAC CHAIR]?

CLIAC CHAIR: So hopefully you all can see it. I believe Heather just put it up.

DR. MICHAEL PENTELLA: Thank you.

CLIAC CHAIR: Can you see them? I just want to make because I can see them. I want to make sure everyone else can.

DR. MICHAEL PENTELLA: All on one page. Great.

CLIAC CHAIR: Perfect. So if the committee wants, please take a second or so to briefly review the agreement, see if there's anything you want to discuss. But I see one hand raised. [CLIAC MEMBER], please go ahead.

CLIAC MEMBER: Thank you. I just wanted a clarification on what we mean when we say that prior to purchasing equipment must complete a risk assessment analogous to analytical verification. So the analytical verification occurs when you have already purchased the instrument and you have on site to play around with. With most of these purchases, you might have the opportunity to go to an AACC symposium to see the instrumentation. But no, as far as I know, no vendor is really willing to drop a half million dollar instrument into the lab so you can play around with it. And so I guess I would like a little bit clarification on what we mean by the risk assessment, theoretical or actual because that's very vague.

DR. MICHAEL PENTELLA: And maybe we can clarify that more by saying a theoretical risk assessment because you will have it in your laboratory. But you should go through the procedures that you're going to use to utilize the instrument and think through the steps and what are the risks, what are the hazards through the various steps of the procedures. And I think when we say analogous to analytical verification, you're also thinking through, what do I need to do to verify the use of this instrument? And you're thinking of that prior to purchasing it to make sure that you have the resources you need to do that verification process so we can clarify that by adjusting that language. You think that will help?

CLIAC MEMBER: Yeah. Thank you.

CLIAC CHAIR: Sorry. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: So I cannot thank you for the work. And thank you for the presentation. I had a scope question because as it stand right now, I know we do biosafety risk assessment on new things that come in the lab. And annually, I know I have to sign those. But is this specifically for instrumentation. Is that the scope of the workgroup as opposed to just the general biosafety in the laboratory?

DR. MICHAEL PENTELLA: We focused on instrumentation in this workgroup and the use of the instrumentation and the risk that may present. But some of this, like the better defining what goes into a risk assessment, can be for the entire biosafety plan for your facility because one of the things that we discussed as a workgroup is that interpretation of what a risk assessment is is different for different laboratories. And by having a definition of what it is, then you could use that definition when looking at instrumentation and use it for other procedures in your laboratory as well.

CLIAC MEMBER: So the reason I'm asking about the scope and the instrumentation-- and I think you guys alluded to that because if I look at number 5, the lab may decide to approach safety or decontamination one way that's going to invalidate the way the instrument's supposed to be handled. And so I don't know how you can have a specific definition and the specific guidance. But every instrument, if those are not-- if that's not already part of the FDA approved approach to that-- I'm wondering how if we're going to put the lab into situation that they can't really get out of-- so I'm curious to just hear from others, how do we manage that?

CLIAC CHAIR: Thank you. [CLIAC MEMBER]?

CLIAC MEMBER: Hey, appreciate it. Opportunity to ask some clarifying questions. So this goes back to, I think, what [CLIAC MEMBER] was asking about earlier with regards to the risk assessments. So one question for clarification from the working group is whether or not this risk assessment for equipment and instrumentation would mimic that of which what we are doing for pathogen-specific or methodology type of risk assessments. I do envision this might be a little bit different. So I don't know if the working group had discussions on what those risk assessments would look like and whether or not they should mirror or refer to these pathogen-specific or method-specific risk assessments that are currently being done. So that's the first question. I have another as well.

DR. MICHAEL PENTELLA: So what the workgroup discussed is a risk assessment for instrumentation throughout the laboratory, not just the microbiology area, where you may be working with specific pathogens. So we would assume that-- you would look at the blood sample, for example. And what pathogens would you expect to encounter in that blood sample? And then take that reasonable steps to that risk assessment process. So I would say that this would be a risk assessment that we were discussing that is not pathogen based. It's looking at the global risk of encountering a pathogen in a sample.

CLIAC MEMBER: Thanks, Mike, and agree on the pathogen side. I think the other component that I had there was method specific. And I think you're answering that as well, so not just looking at microbiological and pathogen but actually looking at the actual principles of the assay and the method and looking at that as well. Thanks. And then one other one with regards to clarification on risk assessments is looking at adding it to the CFR. That would then be auditable by CLIA, correct? That is the intention?

DR. MICHAEL PENTELLA: That is the intention that the CLIA audits would include looking at risk assessments, would include looking at competencies for individuals, for biosafety practices. So it would be much more inclusive for biosafety practices than it is now.

CLIAC MEMBER: Thanks. That's all the questions I have on risk assessment. There's one more on another one. But I'll pause there to let others ask. Thanks.

CLIAC CHAIR: Great. Thank you. [FDA EX OFFICIO]?

FDA EX OFFICIO: Hi, Courtney Lias, FDA. I wanted to acknowledge that number 5 appears to be a recommendation that FDA impose requirements on manufacturers to add information on disinfection of instruments to their labeling or as part of their instrument instructions. And this is a request that we've heard in a lot of forums other than CLIAC. And I think we understand why that would be a good approach for manufacturers of instruments to take to make sure that people understood how to effectively clean and disinfect the instrument if they needed to without breaking the instrument. It's very difficult for a laboratory to do that without an understanding the design of the instrument and materials that are used inside. So we are currently working and talking with CDC on this. We have been talking with CLSI on this. And also, we have recommended to the Medical Device Innovation Consortium called MDIC that they tackle this project. They are currently considering whether they want to do that. So I mean to say that to say we support this issue. But my main point here is that FDA requirements are not under CLIA. They're under the Federal, Food, Drug, and Cosmetic Act. And so recommendation number 5 is not under CLIA's purview. So I note the recommendation and the desire for FDA to help in this area. But I would recommend that CLIAC remove number 5 as one of the recommendations for that reason not because it's not important but simply because it's not a CLIA requirement. Thanks.

DR. MICHAEL PENTELLA: Thank you for that explanation. And I am really happy to hear the progress that's being made as well.

CLIAC CHAIR: Thank you for that clarification as well. I was certainly under the impression that CLIAC could have recommendations, so any of the three agencies that are part of the CLIAC. But we can certainly figure that offline. And I appreciate the comment that you've already-- are addressing that as well. One thing I will say before I go on to the next question is, obviously, because of some of the things [FDA EX OFFICIO] brought up, a lot of this burden will fall on the manufacturers. I think it's appropriate to have the laboratories do their own risk assessments. But risks of aerosolization inside an instrument or things like that, we as end users won't know. That's really got to come from the manufacturers for that information. So I know it's littered throughout these agreements. But highlighting that regulatory manufacturer end user partnership in this is going to be really critical for success.

DR. MICHAEL PENTELLA: Absolutely. And that was discussed quite a bit, [CLIAC CHAIR], because we're looking to the manufacturer to provide a lot. But we want the end user to have information of what they should be asking for as well. So by adding that gives them a bit of authority to ask those questions of the manufacturer.

CLIAC CHAIR: Thank you. [CLIAC MEMBER]?

CLIAC MEMBER: So my question was somewhat similar because I knew FDA really couldn't make manufacturers do certain things, Mike, although I'm concerned about a lot of stuff falling on the lab, like [CLIAC CHAIR] said, where they're not expertise enough to know what's going on. However, I do think manufacturers wouldn't mind having that guidance. And I know in the past, for instance, when we had GI multiplex, we asked manufacturers in their use packets that they still recommend to collect culture at the same time that they're doing their multiplex. So I do think that they're amenable to those recommendations. I do think it will be very hard for certain labs to do it as what [CLIAC CHAIR] said. So I think it's good to keep the dialogue open and that manufacturers typically will go to a site and say what do you like? What do you not like? And they get that information feedback. I just think it is a recommendation we can put forward to them for sure. The other thing is will this apply to CLIA waived sites as well? I mean, they're not using a lot of particularly intricate systems although we're getting more and more molecular and more. And it's a specimen that could be contaminated with whatever and spray it all over, having been a director of a CLIA waived site as well. So I'm just wondering where that falls too. And I don't think we should ignore that. So that's my comments. Thanks.

DR. MICHAEL PENTELLA: Thanks, [CLIAC MEMBER]. We didn't intend this to be only high complexity or moderate and high-- we intended to be all laboratory locations. And your point is well taken. And the need for education and training is in these agreements as well so that laboratories will learn more about the risk assessment process, will learn more by having competency assessments and will broaden the knowledge base throughout the laboratory environment. And that will grow that culture of safety that we want to improve in all these clinical labs.

CLIAC CHAIR: Great. Thank you.

CMS EX OFFICIO: If I could just-- sorry, if I could just add there. So this regulation 1101 falls under subpart J. That would not apply to certificates of waiver.

DR. MICHAEL PENTELLA: Thanks for that information. Would we need to put it someplace else, [CMS EX OFFICIO], to apply?

CMS EX OFFICIO: We need a statutory change because we're really limited in our ability to provide oversight to the certificate of waiver labs.

DR. MICHAEL PENTELLA: Thanks.

CLIAC CHAIR: [CLIAC MEMBER], I know your hand's still up. You said you had a follow-up question. Then we'll go to [CLIAC MEMBER] and [CLIAC MEMBER].

CLIAC MEMBER: Yeah. Thanks. So this actually goes back to [FDA EX OFFICIO] comment. And regarding agreement number 5, Mike, did the workgroup consider the current landscape-- and I know you all had talked about manufacturers. I really appreciate that and understand that. However, with the final rule of the FDA and LDTs, laboratories are now also manufacturers. And so laboratories that are utilizing and creating, I guess, if you will an LDT or modifying are actually not the manufacturer. So what the requirement or the intention of the workgroup have-- the requirement of laboratories actually providing the biorisk assessment information as part of that submission to FDA-- thanks.

DR. MICHAEL PENTELLA: The workgroup did not discuss that potential. We did not discuss the LDT rule. And I also recognize that if manufacturers put instructions for cleaning and decontamination and a laboratory chooses to change that, then they have to go through and apply at the FDA under LDT. But we didn't get into that on this discussion with these questions.

CLIAC CHAIR: Thank you. [CLIAC MEMBER]?

CLIAC MEMBER: I'm reading the first sentence of number 3 as we're sitting here discussing this important topic. But that sentence is open for all kinds of abuse or all kinds of burden on the laboratory. What does it mean to perform a risk assessment? Is it just biosafety? Or is it the entire risk that a device or an instrument might project on the laboratory? And I suggest that a good laboratory that cares for the safety of its employees might have done this already. And how do we fulfill this obligation is really my question?

DR. MICHAEL PENTELLA: Well, we as the biosafety workgroup focused on the biosafety risk assessment. So we could add that term to number 3, so biosafety risk assessment.

CLIAC MEMBER: That would be helpful.

DR. MICHAEL PENTELLA: And by defining what that risk assessment should include, then we can better standardize what laboratories are doing and make it easier for them to do the process-- to perform this process. So we want to educate, train, and make it easy for people to do the biosafety risk assessment. And we'd like them to be at least doing a virtual assessment before they purchase it.

CLIAC CHAIR: And along those lines, one thing I would add-- and I'm trying to keep track of all the modifications we've been discussing so far. But one thing I would add as a potential-- well, I guess, it wouldn't be an agreement. But a recommendation would be-- assuming this gets approved, the creation of a form or a training document or training webinar, providing some guidance to laboratories on how to perform these biosafety risk assessments-- I appreciate that number 3 is broad. We like things that are broad because a lot of room for interpretation but also being able to focus and giving laboratories what's the first next step would be a great tool as well.

CLIAC MEMBER: Exactly.

CLIAC CHAIR: [CLIAC MEMBER]?

CLIAC MEMBER: Yes. Through your presentation, I was listening for one particular point of discussion and did not hear it. And I wanted to wait until we were fairly deep into the discussion before asking this, which is manufacture and validation of instrument warranties. This has come up rather pointedly three times. The first was during the Ebola sequence. The second was during SARS-CoV2 and then just most recently with Marburg virus. And I think the biosafety assessment for laboratories using instrumentation hits the wall when there's a question of the instrument being invalidated should a specimen with a highly contagious, particularly hemorrhagic virus being put through it-- and we've gone round and round in regional discussions-- this being the New York State Laboratory Leadership Consortium-- as to both what the biosafety conduct and the laboratory should be, which is the purview of your workgroup, and the relationship with the manufacturers as to when the instrumentation is invalidated, either through the agent itself or through the decontamination process. And particularly with the comment from [FDA EX OFFICIO] about what is the jurisdiction of CLIA and CLIAC and what is the jurisdiction of FDA, I bring the question forward openly, which is, where does this issue land and how do we deal with it from the laboratory perspective, which is your workgroup?

DR. MICHAEL PENTELLA: [CLIAC MEMBER], we had a lot of discussion dating back to Ebola and the lack of recommendations from manufacturers on how to decontaminate their instruments and also their lack of willingness in some instances to service the instruments if you test the patient with a high-consequence pathogen. And we found that no

one has that ultimate accountability, responsibility to hold the manufacturer responsible or the manufacturers themselves stepping up to the plate because this costs them money to do this. And it's so difficult to find in their documentation at times-- and sometimes it's not even in the documentation how to decontaminate instruments. And that's why we're trying to build a groundswell of laboratorians asking by doing their own risk assessment, what do I do if I test a high consequence pathogen on this particular instrument? So that will put the manufacturer in the position of needing to answer that question. There was a recent paper published where they contacted 13 manufacturers and asked them, what should I do to decontaminate my instrument after a high-consequence pathogen is tested on it. And they only had 3 of the 13 respond back. Consequently, we're at a very similar spot to where we were in 2014. And the efforts of this workgroup, which we don't have the authority to do that-- CLIAC doesn't have the authority-- was to build the end user into the system to be asking those questions before using this instrumentation. So does that address what your thoughts are, [CLIAC MEMBER]?

CLIAC MEMBER: I'm not sure because-- and again, this is from personal-- I'll call it regional experience because this was discussed at great length three times amongst the New York State Consortium is the biosafety protocols can be followed. The decontamination per manufacturer recommendation can be followed. The warranty is still jeopardized, hence placement of instruments in a pathogen laboratory for patients of high concern. The problem is a patient with a hemorrhagic fever can present anywhere in the health system. And their initial emergency department evaluation samples can run through the main lab. And the resolution at our consortium discussion-- and since this is the public record, this is the New York State Laboratory Leadership Consortium, which has been meeting monthly since April of 2020 and is a forum for discussing issues pertinent to laboratory operations amongst the 13 academic medical centers of New York State. And particularly when issues like this come up, we aim to have New York State Department of Health on the line. The resolution of this particular discussion about Marburg virus was-- what it hinges on is identification of a patient at risk because a low-risk patient in the emergency department samples' going through the main lab is of sufficiently low risk that this invalidation concern does not come up. But a patient of high concern-- and there are criteria for declaring that-- then gets the treatment both of secure transport and very prioritized and selective initial evaluation through laboratory testing and work with the appropriate public health laboratory for the specimens. And that was, in essence, our discussion to navigate this issue of when is a patient of sufficient concern to potentially invalidate your instrument. That was where we left it in our most recent discussion, which was only three months ago.

DR. MICHAEL PENTELLA: I see a big risk, though. And that's relying on the physician identifying that patient.

CLIAC MEMBER: Correct.

DR. MICHAEL PENTELLA: --early on.

CLIAC MEMBER: Correct.

DR. MICHAEL PENTELLA: As we know, that does not always happen. What the workgroup discussions around it is being prepared for that before it happens.

CLIAC MEMBER: Thank you. Because that is the risk assessment. And that is precisely the landing zone for that risk assessment.

DR. MICHAEL PENTELLA: Anywhere in this country, someone could have a patient be positive for Marburg today, Lassa fever today. So consequently, we all have to be ready. And we have to ask that manufacturer before we purchase that instrument, am I going to be able to test this sample on this instrument without invalidating my warranty, without losing the use of it? Is it safe to use for other patients then? And we have to have the end user be prepared to ask those questions because there's nothing that is a requirement of the manufacturer to make that happen.

CLIAC MEMBER: I'm in agreement with you. What I would add to the record is the risk assessment includes working with the emergency department. It's not just a laboratory exercise. It's a risk assessment of patient intake.

DR. MICHAEL PENTELLA: Absolutely. Has to be a risk assessment for everything you're doing in your facility, from drawing the sample all the way through to discarding.

CLIAC MEMBER: And in prior CLIAC discussions, we've asked the question, where does the lab responsibility begin and, therefore, where does the CLIA accountability begin? So what I'm bringing to this floor is a regional discussion, which makes clear that this is a team effort.

DR. MICHAEL PENTELLA: Yes.

CLIAC MEMBER: Thank you.

DR. MICHAEL PENTELLA: Thanks.

CLIAC CHAIR: Thank you. [CLIAC MEMBER]? I think you're muted, [CLIAC MEMBER]. Can you hear me? You're muted.

DR. MICHAEL PENTELLA: [CLIAC MEMBER], you're on mute.

CLIAC MEMBER: Trying to get off.

CLIAC CHAIR: There you go.

CLIAC MEMBER: Sorry. Wasn't clicking fast enough. No, I agree with [CLIAC MEMBER]. The assessment has to be done prior. And we went through this with a lot of Ebola scare in Rhode Island. And it was crippling for us. But the reason I'm raising my hand is actually related to what was said before about the CLIA waived sites and that they wouldn't be applicable to this safety biosafety conditions. And that concerns me not just in the CLIA waived sites. But [FDA EX OFFICIO] just mentioned that we're trying to do more things at home, et cetera, et cetera, which I knew this would come. And what are we doing about safety at home too? So I don't think we can eliminate the CLIA waived or the at-home testing as far as safety in some way. So I don't know how to get it in there. But I think it's something important to address because it's only going to get broader and potentially more complicated and more likely to have contamination, so anyway.

CMS EX OFFICIO: There's really no choice in that. Home tests are beyond CLIA. And the certificate of waiver, we simply don't have statutory authority. It takes an act of Congress for us to have that authority.

CLIAC MEMBER: So I'm wondering, can something more fall into the manufacturer's realm for decontamination or biosafety or anything like that? [FDA EX OFFICIO], you mentioned that when we try and use non-toxic agents, et cetera, et cetera, in at-home tests. But I don't know what that basically means.

CMS EX OFFICIO: And not to speak for [FDA EX OFFICIO], but, again, as she mentioned earlier, this is a CLIA advisory committee. So we need to keep our recommendations to CLIA.

CLIAC MEMBER: But we're ignoring a big population. That's it.

CLIAC CHAIR: [CLIAC MEMBER]?

CLIAC MEMBER: Hi. I hear the conversation. And I was part of the workgroup. So I understand the stress on the importance of the risk assessment. But as we talk through the elements of the risk assessment, a large emphasis is being placed on reaching out to the vendor and asking them to provide information that's critical to the success of performing the risk assessment. However, CLIAC and CLIA has no impetus. We have no ability to force the vendor to provide this information. The lab is forced to ask the vendor for this information. However, if we place regulatory requirement upon the lab to perform a risk assessment that really is required to need this information, I think we're applying pressure evenly upon the lab from two different angles. Does that make sense? So unless we temper this a little bit, I'm afraid that we're placing the labs in a uncomfortable position.

CLIAC MEMBER: It's a lot of work too.

CLIAC MEMBER: Yes. And I guess, to that point, risk assessment is a pretty complicated document to complete and complete it accurately. And I don't know that most labs, especially moderate complexity labs, are truly prepared to complete a risk assessment the way it should really be prepared.

DR. MICHAEL PENTELLA: Well, there are trainings out there and available further for free that can train people on how to do a risk assessment. And you want to start somewhere, trying to build people's ability to develop the critical thinking skills that they need to handle things safely. If you have a high-consequence pathogen go through your laboratory, the results are going to be that you're going to have a lot of people being monitored for signs and symptoms of illness for a good period of time. And that's going to create a lot of stress in your laboratory as well. So it's better to have thought through it by doing a risk assessment ahead of time than to be faced with an emergency on a lot of-- placing people in difficult situations who may decide to walk and go to other job opportunities so they don't face this type of exposure.

CLIAC MEMBER: So perhaps there's a runway to be built with competency, assessment, training, and collaboration so that we're building a runway for success instead of throwing everyone in at the deep end.

DR. MICHAEL PENTELLA: And maybe there should be a phased work plan to bring this about because we do list number 8, the competency assessments. And maybe we need to have a plan of how laboratories could implement this requirement and that could be developed.

CLIAC CHAIR: I think it's a really good call out because to [FDA EX OFFICIO] comment before about bullet number 5 in terms of it being out of scope of CLIAC-- that is outside of our purview here. But in the absence of that, [CLIAC MEMBER] point really holds true. If the manufacturers aren't required to provide this information, the laboratories could have a really hard time doing a complete assessment. They certainly can do an assessment. The question is how complete will it be. But what I don't know is if there's any changes to the CLIA regs or standards that would then make it part of CLIA and, therefore, more circular logic that may have more footing to make it in scope in terms of a recommendation. But either way, future potential-- so I think it's just something as we start talking about recommendations. How do we resolve that in the absence of the lever to force manufacturers to participate in this? I suspect they will. But that may be overly naive. And certainly, there'll be a spectrum. Some will. Some won't. We'll just have to resolve it when we get into the deliberation of the recommendations.

DR. MICHAEL PENTELLA: I think number one is the most important, and that's to have that standardized definition of a risk assessment. So we require that everybody perform a risk assessment to the same degree. So then we have consistency. If manufacturers know what we're asking for, then they'll do their best to meet it because they want to sell the equipment.

CLIAC CHAIR: And I suspect it could be relatively high level. Is it a closed system? Is there a risk of contamination of the instrument itself by pathogens? Is there risk for aerosolization? It doesn't necessarily have to be pathogen specific but just those general risks of contamination and risks to the end user. [CLIAC MEMBER]? Go ahead.

DR. MICHAEL PENTELLA: Well, I was going to add, we also have to think of the people doing maintenance on it. So even a closed system at times has to be open and there is the risk of exposure.

CLIAC MEMBER: So I was just going to make a comment. But I think [CLIAC MEMBER] beat me to it. I think what we don't want to do is put all this pressure on the labs to do these things when they may not have all of the tools that they need to do that. So I'm wondering, instead of requiring-- I think we're using the word required a lot in here-- if we can have more recommendations for the labs to do that. And I like the number one way you need to define this. Actually looking it up, the CDC has a biosafety in microbiology on the BMBL document, making some recommendation for labs to look at this document and develop a biosafety risk assessment but not necessarily making it a requirement, particularly when it comes to instrumentation. So just wanted to reiterate what [CLIAC MEMBER] was saying to not put this pressure. The second thing I wanted to ask, though, is this something where we also take into consideration OSHA's requirement for safety of lab workers? So I don't know if you guys consulted that document. Is there some guidance there that we could use as we're trying to make these recommendations?

DR. MICHAEL PENTELLA: You're referring to the general duty clause to provide a safe working environment for the staff?

CLIAC MEMBER: I was looking at the OSHA bloodborne pathogen standard.

DR. MICHAEL PENTELLA: The bloodborne pathogen standard.

CLIAC MEMBER: So if something like that exists, then we can maybe build on-- and the other thing I wanted to mention is I know we're talking a lot of about pathogen. But one of the things that we had to deal recently with was prion. Yes, it falls under-- considered pathogenic, but it was that moment where micro has a process and biosafety risk assessment. And we know how to deal with this. But we had no our flow lab who never has to think about this kind of thing. So keeping in mind the instrumentation, yes, for microbiology, I think we are sensitized to it. But this guidance will apply to all lab instrument and that can be a big deal. So again, being careful how we word this so not to create more pressure on the lab but definitely important.

DR. MICHAEL PENTELLA: I think it's important for us to recognize that more than just microbiology needs to do a biosafety risk assessment because there are samples that contain pathogens throughout the entire testing system.

CLIAC CHAIR: Thank you. [CLIAC MEMBER], I'll call on you. I just want to call out-- we have around 25 minutes left in this session. So after [CLIAC MEMBER] comment, I want to try and focus us on our final recommendations. Now, again, we can wholesale approve-- take the agreements and put them forward. I am hearing that there's some clarifications that can be added to the workgroup agreement, such as reiterating the scope of this to the instrumentation piece. There was a comment about it that the-- I don't know if theoretical is the right word. But the risk assessment being done obviously before the instrumentation is in the laboratory, at the time of consideration of purchasing-- and there was a comment before as well as in the chat about some kind of guidance document or guidance webinar on what would be the

appropriate risk-- what would that risk assessment look like? So just food for thought because I'll start to pin us down to making some formal recommendations. But before we go there, go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I just wanted to-- point of clarification, when we talk about competency, we are talking a general competency that would apply to multiple instrumentation. We're not saying that we're going to develop and require individual competency for each kind of instrumentation. So there wouldn't be one for the chemistry analyzer in your lab, one for your hematology analyzer.

DR. MICHAEL PENTELLA: It would be a general biosafety competency that would cover all your instrumentation in the laboratory. Now, you could get more specific for some specific instruments. But you could have both the general biosafety competencies, in which there is a document from CDC on biosafety competencies from 2015. So you could adopt those. But you could make them more specific for your particular equipment and your laboratory. It would be your choice and dependent on how you do your competency assessments.

CLIAC MEMBER: Could we just put general in front of biosafety for line 7? Because what I'm envisioning is somebody interpreting that to mean that, within the employees file, there should be a biosafety training for each piece of equipment that they rotate on.

DR. MICHAEL PENTELLA: So in number 7, you'd like it to read, the workgroup agree the CLIA requirements should be revised to include general biosafety training.

CLIAC MEMBER: Yes, please.

DR. MICHAEL PENTELLA: That fits the consensus of the workgroup.

CLIAC CHAIR: So I'm not seeing any more hands raised. So let's see if we can distill this down to a draft recommendation. Again, reflecting back to the group, it feels like we are in the refining phase and not negatively reacting towards the workgroup agreements in general. So it's really more about refining scope and using some additional words or verbiage. [CLIAC DFO], I don't know if you've been able to document the ones we've mentioned so far, like the general scoping its instrumentation, the word theoretical. And I will actually defer to the ex officios or the rest of the group as to, do we have to totally eliminate number five due to a scope issue? Or if there's a way it could be reworded where it could be in scope. Courtney, if you've got-- you're obviously probably the best one to give us guidance.

FDA EX OFFICIO: So I think the challenge for scope from my perspective is that this would require an FDA regulatory action and not a CLIA regulatory action. But it sounds like the goal really relates to having manufacturers work toward providing support for laboratories by validating instructions for cleaning and disinfection. So consider a CLIAC recommendation to the manufacturing community to do x, y, or z with respect to validating cleaning and disinfection instructions in their labeling. And cleaning and disinfection is what the official wording would be with respect to the labeling and an FDA label. That's a suggestion.

CLIAC CHAIR: Thank you for that. And I wanted to split it up as well because there was the cleaning and disinfection component. But I think we're also asking manufacturers to provide some information about general risk assessment. I know I keep using the word, like "closed system utilization." But that's what I would want from them to say, hey, in this reaction chamber, there's the risk of aerosolization that aerosolization could potentially impact an end user.

FDA EX OFFICIO: I think, though, the ability to what's called decontaminate here-- or what we call cleaning. In addition to what you're saying, which I think is fine, is dependent on the types of agents you can use on that instrument, you might actually damage the instrument or cause leaching of chemicals out of the instrument into the reagents or breach the plastics inside if you use the wrong chemicals. So that's a lot of times what a manufacturer will look at is which types of agents and what process you use to do a decontamination. And they also, in a lot of cases, are going to have to work toward designing their instruments-- be able to be cleaned and disinfected effectively.

CLIAC CHAIR: And I think you mentioned it before, a lot of times the cleaning and disinfection are quite complex. You need a field service specialist to come out to do it. Or laboratory personnel cannot. Sometimes requires to actually partially disassemble the instrument. [CDC EX OFFICIO], you have a hand up?

CDC EX OFFICIO: Yes. Hi. Can you hear me?

CLIAC CHAIR: Yeah.

CDC EX OFFICIO: Just a point of clarification on the agreement number five. As we discussed, these agreements-- I would like to remind everybody that these were the workgroup agreements and now the committee should actually

develop specific language for each recommendation. In other words, the agreements that are presented now on the screen are the formal output of the workgroup. So I just want to make sure we clarify that rather than changing the wording of those agreements that are on the screen right now. So, [CLIAC DFO], thank you for starting a draft CLIA recommendation list underneath. Over.

CLIAC CHAIR: Thank you.

CLIAC DFO: And I will clarify that, for instance, if everyone looked at this and said, this is perfect, then, yes, you could say the CLIAC advisory committee accepts all of these workgroup agreements as a recommendation. But since there is a discussion around each one, then we should put forward recommendations related to those changes that you have discussed.

CLIAC CHAIR: Excellent. So, [CLIAC MEMBER]-- and then I say, [CLIAC DFO], I guess we could start dropping down each of those lines to the recommendations. And we could do some minor scoping. Again, I want to caution against precision of wordsmithing. But meaningful wordsmithing, we obviously we have to have that conversation. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: At risk of returning to the same topic-- but it's the underside of the discussion-- is these are recommendations for education and preparation. These recommendations do not make any statement about documentation, auditing, addressing failure points. And the repetition is if the wrong decontamination process is used, now what? In other words, does that then have consequences for instrumentation, status, and/or the validity of the instrument for future use, which leads to the fourth of four points, which is validation of the instrumentation after the disinfecting procedure. So I haven't heard discussion of, in essence, completion of the cycle. This isn't pushing a product out there but without the backside of verifying that these things are done properly. This is a question, not a recommendation. Does the virtuous cycle of assessment and correction constitute part of this workgroup's purview? And should it fall into any CLIAC recommendations? I myself don't have a recommendation as such. I'm asking the question.

CLIAC CHAIR: Thank you. Any thoughts on that?

DR. MICHAEL PENTELLA: That did not come up in our discussions. And we did not look to the continuation of this over multiple periods of time. We establish it to be put in place. And if these things occur, they can be part of the auditing process. And that gives you some continuation. But we didn't go in that direction.

CLIAC MEMBER: And I think there's risk in this discussion saying and here's the whole regulatory framework for making sure you're doing everything you're supposed to do because I don't perceive that was within the scope of this workgroup. It does hang in the air, though.

CLIAC CHAIR: So I see [CLIAC DFO] busy reorganizing the agreements into recommendations. I think some of those suggestions have already been included. Why don't we just start going through them one by one as she's refining them? How does everyone feel about one? And we're not voting now. We're discussing. But does one reflect the conversation to this group so far? Not hearing any-- seeing anyone raising their hand, I'll assume, yes. How do we feel about 2? 2 looks like it was a combination of the original agreements 1 and 2. We're now being subverted. So take a second, please read number two. Any questions or comments about 2? I was thinking a little bit. I think it's maybe too much of wordsmithing. I think it's fair to say that the laboratory has a responsibly to request that information. Obtain is not up to us. It's the terms of the manufacturer being able to supply it. But I don't think that should-- in the absence of it, I don't think it in the way of a risk assessment. You could still complete a risk assessment without that. It may not be as thorough. But you can still complete it. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I was just a little-- it makes me a little confused that this part a says it should be comprehensive about the risk assessment, et cetera. I get that. But later, we said—[CLIAC MEMBER] had suggested we say it's a general. It's not specific to an instrument. And comprehensive to me sounds like every single detail there. I would say it should cover the risk assessment. Or it should cover the risk assessment including-- I would say including identification of a hazard mitigation management and performance monitoring.

CLIAC CHAIR: I hear what you're saying. I think the key part here and how I interpret the word "comprehensive" before was that it wasn't just calling out the risk. It's calling out the risk and then commenting on what's the mitigation and management and monitoring of it.

CLIAC MEMBER: And I get that. So that's why I said it should cover the full gamut. But comprehensive sounds like it should cover--

CLIAC CHAIR: There a sense of--

CLIAC MEMBER: --everything.

CLIAC CHAIR: I hear you.

DR. MICHAEL PENTELLA: Are you looking for the term thorough risk assessment?

CLIAC CHAIR: I would say at this point, we're probably wordsmithing for the sake of wordsmithing. I think we're all agreeing on the spirit. So I would say let's parking lot it and see if we can go through some of the others. Any other comments on bullet two? [CLIAC MEMBER], is your hand up?

CLIAC MEMBER: I just wanted to comment on the fact that a manufacturer may say we're not giving you that because we want to come out and take care of it ourselves. So I would just clarify that piece that there may not be a role for the laboratory in that disinfection. So I would add that part in there to clarify--

CLIAC CHAIR: That's why we picked the word to request. So you have to ask. It doesn't mean--

CLIAC MEMBER: Request and clarify. Am I doing it? Are you doing it?

CLIAC CHAIR: [CLIAC MEMBER].

CLIAC MEMBER: I was trying to think about this-- requesting the information from the manufacturer, and we're putting it as a standalone bullet. But I think, essentially, that's going to be part of the work that the lab does to do the risk assessment. It won't be the only piece because as we've been discussing, if the manufacturer doesn't have this or doesn't give it to you, you still have to do it. So I'm wondering if there's a way for us to say, the lab has to perform a risk assessment by evaluating ABC, including getting information from the manufacturer or requesting information from the manufacturer, as opposed to making it like, this is your responsibility. You have to do that as a standalone bullet. It should be part of the general work that the lab does, as opposed to just one requirement, if that makes sense.

CLIAC CHAIR: So I think, [CLIAC MEMBER], maybe in that bullet B-- or maybe even make it a sub bullet of A that just part of that comprehensive or general risk assessment includes asking the manufacturer. So you could just make B part of that sub bullet under A. I like the call out because it's basically telling the labs that not all the information must come from them alone. Don't forget, reach out manufacturers. But obviously it doesn't end with only the manufacturers input. I feel like we're getting pretty mature on bullet 2. How do we feel about bullet 3? Go ahead, [CLIAC MEMBER], while we're working on that.

CLIAC MEMBER: Sorry. I thought I put my hand down. I feel like [CLIAC MEMBER] is in my head. So we're pretty much there together.

CLIAC CHAIR: Good. [CLIAC MEMBER], you had another comment?

CLIAC MEMBER: I'm just recalling an earlier discussion comment, which is 3 is perform a biosafety risk assessment. In other words, this is a specific recommendation. So it should be clear what the ask is.

CLIAC CHAIR: Good call. Any other questions or comments on 3? [CLIAC MEMBER], I see your hand up.

CLIAC MEMBER: And [CLIAC MEMBER], just said what I said earlier. So we might want to make sure that this is specifically a biosafety risk assessment. And trying to make this as uncomplicated as possible, I don't know how we can do that for laboratories. And when is this going to be due and what constitutes an adequate biosafety risk assessment? There's a lot of variables here that could be onerous to the laboratory.

CLIAC CHAIR: And I know it's said by a couple of people so far. And I was going to get to it once we got through this 1 through 5. But I think a recommendation to whatever the appropriate agency, likely CMS in this setting, would have some educational output to educate the laboratory community as to what this looks like, what this risk assessment could look like. How are we looking on number 4? [CLIAC MEMBER], I see your hand up.

CLIAC MEMBER: Well, I was just going to say, in order for the-- this is a lot of work for the labs. And as someone mentioned earlier, risk assessment is very complicated. But one of the ways you could actually get some information from the manufacturer is when you're going to purchase it, you don't get the purchase unless you give us the information. So I just think it's something to consider because we have before you implement. So I would just add it as a-- if we're going to make this a mandatory thing with CLIA that they just know when's the right time to ask. And it would be

potentially before the purchase. With purchasing, we don't purchase it unless we know what the risk assessment is for this instrument-- biosafety risk assessment. I don't know, just a suggestion.

CLIAC CHAIR: And is it a comment doubling down on something that's already here? Or are you suggesting adding something?

CLIAC MEMBER: I don't know if you can put in as an example of how to get that information because as Mike already said, they surveyed 13 manufacturers. And they only got three to call them back on this. So I think it's hard to get. So let's make it easier for the labs. A suggestion. I don't know where to put it. I just think I'm thinking if I have to do this, when am I going to ask for it to prepare, as [CLIAC MEMBER] said, for the inevitable.

CLIAC CHAIR: Yeah, I see what you're saying. I would say right, ideally, and it is commented here kind of before or during the purchasing process. But obviously we already have a lot of instruments in our lab, and you may miss that-- you may miss that time point as well. I still do strongly believe that even in the absence of a manufacturer providing meaningful information, you can still carry out a biosafety risk assessment alone. Again, may not be totally thorough, but it's going to be best you can with the information you have. So it's-- I still think it's doable without their participation. I do think, especially if this becomes a clear requirement, that this will-- that manufacturers will-- majority of manufacturers will likely start to provide such information. They only have to do it once and just hand it out to the laboratories that purchased their equipment. Any other comments on bullet 4? OK, hearing none, I'll assume everyone's in agreement. How about bullet 5?

CLIAC MEMBER: Doesn't really go anywhere.

CLIAC CHAIR: Yeah, I was just going to make that comment. It's not directed to someone or-- it's a really good-- the spirit behind it is very meaningful and powerful.

CLIAC MEMBER: Right, but it doesn't go anywhere. Yeah. Yeah.

CLIAC CHAIR: [CLIAC MEMBER], I see your hand up.

CLIAC MEMBER: Yeah, so just for clarification, again, just considering what was discussed earlier with regards to scope of this and going back to my comment about, again, the LDT rule, which I know the working group has said that they did not consider that. My concerns still are there with regards to-- regarding the rule. And if there is an LDT, then the laboratories are going to be forced to do this. And we've been discussing potential collaboration and coordination with manufacturers. However, if they don't actually provide that, then where are we? So I guess my question is really about clarification on where we stand and whether or not this is something that we are requesting that FDA actually goes through and makes this a part of the approval or clearance process.

CLIAC CHAIR: Yeah, it's challenging because I know the LDT rule is technically out of scope of our purview of discussion here. I would say in that rubric, the laboratories are manufacturers, and they would be the ones that would have to, I guess, provide that information to themselves as both the manufacturer and end user. But again, I feel like I'm treading in very thin ice right now in terms of what is in scope of our conversation.

CLIAC MEMBER: Yeah, and just real quick clarification on that as well as far as I understand it as well, Jordan, is that the laboratories, being manufacturers, would actually have to submit this as part of their package to the FDA for clearance. So it's beyond the lab to lab and lab to itself. But you'd have to provide this to the FDA. And that's where I'm concerned is the ability of the laboratory to be able to do that.

CLIAC CHAIR: Yeah. So I think to [FDA EX OFFICO] point before is that that would be the relationship between the FDA and the manufacturer, which is certainly out of scope of our conversation and actually under a completely different legislative act as well. So that's where those changes would potentially have to be. And if I understand correctly, that's-- I don't know if this type of biosafety risk assessment is part of that communication or submission packet already. Either way, I think that element is probably pretty deeply out of scope of what we can do. OK, well, I think this is pretty impressive. It's 2:15, or 3:15 right now in Eastern. And I think we did a really good job taking these agreements, modifying them with our input. And here we have them. We kind of went through them all already. And it feels like we're at a pretty mature state with them. So we can consider moving forward and going through a motion, seconding and approving and voting. So does anyone have a motion for these draft recommendations 1 through 5? [CLIAC MEMBER]?

CLIAC MEMBER: I'll be parliamentary for just a moment. I will move that the recommendations 1 through 5 be accepted in full with a single vote.

CLIAC CHAIR: Thank you. Do we have any seconds?

CLIAC MEMBER: Second.

CLIAC CHAIR: Thank you.

CLIAC MEMBER: Although I'm sending [CLIAC DFO] a comment. [CHUCKLES]

CLIAC CHAIR: OK. Is it a comment that we need to discuss and deliberate on?

CLIAC MEMBER: No, I think it's just she has in bullet 2, "laboratory should consider the provision of the written disinfect instructions practices as a condition of purchase." Again, it may be that they clarify that because they may not allow you to do it. It may not be something-- No, you don't do it. We come in and do it for you. So I just want to make sure that that's clear. You know what I'm saying, [CLIAC MEMBER]?

CLIAC MEMBER: In the parliamentary procedures, this is a friendly edit.

CLIAC MEMBER: Yeah, it's a friendly edit. [CHUCKLES] We don't want to piss off the manufacturers.

CLIAC MEMBER: No, it was more to say that we won't buy your instrument if you don't provide us with the written material. [LAUGHTER]

CLIAC MEMBER: To do or not to do.

CLIAC CHAIR: [CLIAC MEMBER], I see your hand up.

CLIAC MEMBER: Yeah, I think this is also hopefully a minor edit. Just the sequence-- it looks like number 5 maybe should be number 3 so that we know how to perform biosafety risk assessments before we're told that we have to perform biosafety risk assessments.

CLIAC CHAIR: Fair enough.

CLIAC MEMBER: So I was the one who made the motion. I modify the motion with the comments as given.

CLIAC CHAIR: Thank you. Do we have a second?

CLIAC MEMBER: I don't think I can second my own change. [CHUCKLES] I'll second it.

CLIAC MEMBER: Actually, you can.

CLIAC MEMBER: OK, good.

CLIAC CHAIR: OK. And then so please vote electronically with raised hands. All those in favor, please raise your hand.

CLIAC MEMBER: Not to be difficult, but with that change, point 2, bullet 2, no longer makes sense, really.

CLIAC MEMBER: Yeah, you do have to put something additional into it.

CLIAC CHAIR: To be captured-- to be captured by [CLIAC DFO] in the—

CLIAC MEMBER: Yeah.

CLIAC MEMBER: Yeah. They should request the provision of written disinfection in practice.

CLIAC MEMBER: Well, that's already part of 1. The intent of point 2 was to suggest to laboratories that they make the vendors' provision of the instructions and practices a requirement of the purchase of their products.

CLIAC MEMBER: Yeah, OK.

CLIAC MEMBER: And if the disinfection is not required, they need to tell them that, that we will do it. It's really more that. Are we doing it, or are they doing it, too? Clarify who's doing it when they purchase it.

CLIAC CHAIR: OK, so with an edit like that, do we have to go all the way-- do we go back to the motion again?

CLIAC MEMBER: I do not think so.

CLIAC CHAIR: OK, then we are at the phase of voting. So everyone, again, raise your virtual hand. [CLIAC MEMBER], I see your comment that your virtual hand is raised but you can't find the button.

CLIAC MEMBER: Tony helped me.

CLIAC CHAIR: Oh, you did? You figured it out? OK, good. All right, well, it looks like everyone-- certainly looks like we have a majority, so thank you very much. It looks like this has passed.

CLIAC MEMBER: Thank you.

CLIAC CHAIR: OK, so we are at 3:19 right now. Why don't we take a 15-minute break, and we will be able to continue at 3:35. And we'll go on to our next and final topic, which will be a Next Generation Sequencing Workgroup report. So operationally, it's going to feel very similar to what we just did. We'll have agreements, and we can decide if we want to agree them wholesale or recommend them wholesale or modify them like we just did. So thank you. Let's take 15 minutes. We'll see you all back at 3:35 Eastern.

CLIAC MEMBER: OK, thank you.

CLIAC MEMBER: Thanks, Mike.

The Next Generation Sequencing (NGS) Workgroup
Nirali M. Patel, PhD

CLIAC CHAIR: All righty. Let's give a minute or so. Just everyone file back in. [CLIAC DFO], what do you think. For the people without cameras, it's hard to tell who's here and who's not.

CLIAC DFO: Yeah, we can go ahead and get started.

CLIAC CHAIR: Yeah? OK. All right, well, welcome back, everyone. We're on our home stretch for today. Obviously, we're meeting again tomorrow. But we're going to close out the day with a report from the Next Generation Sequencing Workgroup. It's going to be presented by the workgroup chair, Dr. Nirali Patel. And this is presentation 6 and report 6A on the CLIAC website. Just as before, after presentation, we'll have some time for public comments, followed by our committee discussion. And so let's get right to it. Nirali, kick us off.

DR. NIRALI PATEL: Thanks. Thanks, [CLIAC CHAIR]. And thank you all for being here to discuss our CLIAC NGS Workgroup report about bioinformatics and its role in the clinical laboratory. Next slide, please, Heather.

This is just a brief history of the timeline that's taken us to get here. Back in 2020, when NGS was first getting implemented in clinical labs at large scales, there was a request for information where the need to define the field of bioinformatics as it pertained to the clinical lab was identified, as we currently have difficulty qualifying these folks as laboratory testing personnel and their expertise is of critical value in the clinical laboratory. Next slide, please.

So again, this is just a bit of background of the actual history of our bioinformatics workgroup. We recruited last year and had four meetings this year and came up with what I think are a pretty concise list of recommendations that we hope the CLIAC group looks favorably upon. And so we'll go to our workgroup charge next. Next slide.

And again, our charge was to make recommendations as to how we could qualify bioinformatics personnel to be CLIA laboratory staff and then fall under the purview of all of our training and competency requirements.

The next slide is our workgroup members who come from a diverse background of public health laboratory, industry, reference labs, academic centers, community centers, and really fostered a lot of, I think, practical discussion. And as you'll see in some of our recommendations, we tried to gear recommendations towards what we think really are those minimum requirements to have bioinformatics staff from a diverse range of backgrounds be properly integrated into the laboratory.

All right, so with that overview, we'll go to our first question, which was, what are the current regulatory requirements and guidelines related to the role of bioinformatics in clinical and public health laboratories performing NGS? Next slide.

I'm going to try not to read off of these slides verbatim. But again, as I mentioned before, bioinformatics are a critical component of the test system. And because they incorporate a lot of IT infrastructure, it's not just our usual HIPAA

requirements and CLIA requirements. There's also information technology requirements and areas that during our discussion aren't really bread and butter for me 90% of my time as a laboratory director. And so I think the discussion of this workgroup really showed that bioinformatics personnel have a lot of overlapping responsibilities with our current clinical laboratory staff. But they also have specialized needs for education and training that aren't currently allowable under CLIA personnel roles.

So our next question was to actually create definitions. Because I think in order for us to identify what tasks and people need to occur within this new subsection of CLIA staffing, we really needed to decide what those critical terms were.

And as we discussed this, we realized that while clinical informatics and health and laboratory informatics are important for CLIA and our eventual transmission of results, we really narrowed it down to-- next slide, please-- really trying to carve out what components of this bioinformatics role are really attributed to the laboratory test performance milieu rather than, let's say, research and development activities prior to clinical application, or downstream activities such as data transfer between institutions and, say, integrated health records. And so we really took a very narrow focus on really those roles that were situated entirely within the laboratory and really had a hands-on responsibility for creating that finalized test output. And we tried harmonizing our definitions, such that we weren't actually limited to those technologies and analytes that we are using today. And so, as you'll see in our definitions and recommendations, we tried to create a really all-encompassing set of terminology that wasn't so broad as to be sort of uninformative. We really tried making it something that we don't need to re-form a workgroup 20 years from now with the next technology or the next slate of biological molecules that we'll be able to evaluate for clinical care. And then finally, our final workgroup question was talking about really what are these minimal educational requirements. And going from previous CLIA experience and the experience of having these staff in our labs currently, we understand that there are two general ways to get into bioinformatics in the clinical lab. One is a very structured, formalized training pathway, and another is our picking up of skills as you are working in the laboratory, as you're exposed to some of these new technologies. And we had, I think, some really spirited discussion around how to be, again, inclusive and acknowledge the variety of experiences that really lead to key members of our team without, again, being too permissive and perhaps opening up roles to folks who may benefit from additional qualifications and trainings, as currently there are no well laid out official certification programs that are acknowledged by CLIA or CMS in this environment because we have not really defined bioinformatics in a clinical laboratory setting yet. Next slide.

And again, we also acknowledge that there are different hierarchies of testing personnel. We know that our laboratory director and technical supervisors need to be knowledgeable about NGS and bioinformatics when their high complexity laboratories are performing these. And so how do we ensure that the laboratory director and technical supervisors do continue to have appropriate oversight for bioinformaticians? And again, understanding that folks under the bioinformatician roles can have various skill sets depending on the actual suite of assays and other members of the bioinformatics team that may be present within their laboratory. It's very different if you have, say, a single bioinformatician helping support a PCR-based, multi-gene panel versus a team of 20 bioinformaticians supporting whole exome sequencing, for example.

And so this brings us to the workgroup question of do the current CLIA regulations apply to the personnel discussed? And this is where we realized that, again-- and the whole reason the workgroup was convened-- is that CLIA currently comes from a very biological wet lab point of view.

And so our bioinformatics teams are more based in what we colloquially call the dry lab-- data interpretation, analysis, execution of pipelines and code. And so where do we define these personnel? And again, what are their educational requirements? And the way we did this is, again, we had a very diverse group of workgroup members. And we asked them to survey not only their internal labs but their professional networks to see, OK, what types of people are currently in these roles? What roles do you have posted yesterday? What roles do you have posted today? What are the roles you think you need three years from now? Again, to make sure that we take a very overarching view of not only the current needs and current staff who we think are eligible, but those who will help us continue to drive clinical lab testing in the future.

And so our first general agreement is that, again, we needed to create a very specific carve-out for those personnel who perform bioinformatics data analysis. And we used the blood gas analysis carve out as sort of a template, again, to allow us to create a set of guidelines that are similar in educational sort of tiering and pathways to those for current laboratory personnel. And also to allow for those tiered responsibility approaches with general testing personnel, a general supervisor who can assess competency, technical supervisors for those difficult questions, and then the laboratory director who, while potentially not being able to execute the pipelines entirely on their own, understands the nuances and limitations of the technology that is being used to deliver these highly complex results. Next slide, please.

Is this-- sorry. As this suite of information, I think, is potentially new to many of us, we did put a lot of, I think, repetitive information in here to really call out, again, the importance of making sure that we understand the specialized

requirements for these folks beyond the biological sciences. Again, a lot of these folks come to our laboratories from backgrounds in mathematics, computer science, software engineering. And so we wanted to make sure that we didn't exclude any potential pathways for entry into the clinical laboratory. Next slide, please.

Oh, I see what's happening. Sorry, Heather. My downloaded slides are slightly different than these. OK, I'm back to where we are. OK, so the workgroup agreements. This is where we decided on three key definitions to include potentially in guidance for updating of regulatory guidance and handouts. And number one was the fact that a bioinformatician is defined as any individual who manages, processes, and analyzes biological data using specialized software. Again, we had a lot of robust conversation of should we use proteomics, genomics, RNA, DNA methylation data? But we realized, again, with CLIA being focused on clinical laboratory testing of biological specimens, we really thought that using the definition of any biological data was really comprehensive and did help us apply the field of bioinformatics to the clinical lab environment rather than the more general medical informatic data transmission of, say, progress notes and things like that. And then for bioinformatics, we defined it as the interdisciplinary field that develops and applies computational methods to manage, process, and analyze the biological data. Because again, the focus on the data that is generated and what is needed to be done to turn that data into an actionable result or part of the test system. And finally, we defined a bioinformatics pipeline as a set of multiple computer programs that may be run in series and/or parallel to automate the process of analyzing biological data. Again, the computers are now evaluating all of the different base pairs. They're doing the mapping, the aligning. And as we continue to get more complex evaluation of the biological molecules themselves, our computer programs will continue to become more and more sophisticated and have additional layers. And so that's why we realized that it was-- it was important for us to stay away from very concrete terms as potentially artificial intelligence or just a software package. We wanted to make sure that this is something that can be flexible for future applications.

The next slide, I think, is where we have our discussion about really the educational requirements. And I'd like to flag a couple of things here because ideally our workgroup would hope that these recommendations, after a lot of debate amongst ourselves, would become a primary recommendation of CLIAC. So our first bullet point here is really to address the idea of the homegrown bioinformatics personnel, which is, I think, the pathway that a lot of us have currently used to qualify existing bioinformatics personnel, which is a person who meets the qualifications for testing personnel, performing high-complexity testing from a biological sciences background. But because of the increasing complexity of bioinformatics requirements in the laboratory, we debated what the ideal time for a person to get hands-on training in bioinformatics applications, such as software deployment, pipeline design, variant analysis, what that timeline should be within the lab. And so we talked about anything on the order of six months to two years. And I think we as a group settled upon two years for someone from a more purely biological sciences background to be qualified as a primary bioinformatics testing personnel to be at two years. Because as I mentioned earlier, one of the concerns about bioinformatics not being currently covered under CLIA is that it does have such a different background in the sort of data sciences and computer sciences realm. And so this was a topic of hot debate amongst our workgroup and will likely become a debate amongst our CLIAC group here and potentially for public comment, if this proceeds forward. And so I really did want to flag that the two years came about because of our acknowledgment that bioinformatics is truly a separate skill set than our more traditional wet lab testing. And then again, to get back to a more traditional, what would it take for someone coming out of school to say I want to be a bioinformatician in a clinical laboratory? What are the courses I could take to plan to become one, rather than learning about it once they're in the laboratory and then making the transition over? We again modeled this along the CLIA personnel regulations, where it is to have a bachelor's, master's, or doctoral degree in a wide range of disciplines closely related to the principles and components of bioinformatics, which are bioinformatics, computational biology, computer science, mathematical science, or data science. And then we recommended that they have at least one year of documented laboratory training, performing clinical bioinformatics in a laboratory performing high-complexity testing. Because again, while you may know the technical requirements of a pipeline, I think the regulatory aspects, as well as the high-risk scenarios of incorrect applications of these, we really thought that in order for these personnel who had potentially never interacted in a health care situation before to get the full understanding, they have a year of experience working in this clinical laboratory testing. And then finally, because we know that new degrees are always evolving, and they're named new things, what is the minimum number of credit hours in different backgrounds that you need? And we settled in again from the current CLIA framework at least six hours of chemistry or biology, as well as 24 semester hours of-- or sorry, I read that wrong-- 24 semester hours, of which 6 must be in chemistry or biology and 18 semester hours that really deal with the core bioinformatics needs of bioinformatics, computational biology, computer science, mathematical science, or data science. And we said that this could be in any combination because we understand that the naming and placement of courses in different universities can be very heterogeneous. And again, we identify this as a growing need. And so we wanted to be mindful of practical applications that wouldn't cause us to unnecessarily exclude otherwise qualified candidates because of more of a clerical concern.

And then finally, because bioinformatics as a field is not actually-- was not even thought of when CLIA was first proposed, we think that there are additional requirements for personnel responsibilities that would apply to these bioinformaticians. And these three recommendations are that these personnel would develop and modify as applicable workflows, algorithms, and pipelines needed for clinical bioinformatics data analysis. They would conduct bioinformatics, analysis, troubleshooting, and resolution, similar to our laboratory technicians who do analysis, troubleshooting, and resolution of

processing errors on the bench. And then finally, follow regulations and institutional policies related to the integrity, privacy, and security of patient and genomic data in databases and bioinformatics workflow processes throughout the testing process. And we made sure to end this with "throughout the testing process" because we do know that the data generated in the clinical lab can be transmitted to outside databases. it can be used in research applications, clinical data mining applications. But again, CLIA is focused on our processes within the laboratory. And so we really wanted to tightly focus on ensuring the responsibility of this data integrity within our clinical testing pipeline. Thank you for that. I feel as though I was both very specific and very general in my conversation. So I definitely would like for you all to ask questions. Because as I said, the workgroup was a very diverse group of individuals who had a variety of opinions. But I think we did try to synthesize them into a very practical and also actionable set of recommendations. So I want to make sure we give you all the ability to move as many of these forward as you think appropriate.

Public Comments

[No Public Comments]

Committee Discussion

CLIAC CHAIR: Awesome. Thank you, Nirali. If I may, I want to reflect back at distillation and want the group to either agree or disagree with the spirit of these recommendations. I want to make sure we have alignment on the spirit of them. Then we could get into the details a little bit. So to reflect back, what I heard was bioinformatics personnel are different. You're calling out that they need to be-- they need to be acknowledged. And you're suggesting both from a precedent perspective as well as potentially content that we have a carve-out similar to the blood gas personnel.

DR. NIRALI PATEL: Correct.

CLIAC CHAIR: You're also recommending that we leverage the existing tiers that are commonplace in CLIA in terms of titles from personnel, supervisor, or whatever, but as well as the educational requirements that go along with each of those title tiers. And finally, acknowledging that for these folks, the non-biological science education is part of their education, part of what makes them competent, and to acknowledge that as meeting educational requirements.
So I'll pause there for a second. And well, first off, fair reflection?

DR. NIRALI PATEL: Fair reflection. Great, great summary.

CLIAC CHAIR: And so I'll pause there. And anyone have any supporting comments or anything against the spirit of what is recommended? So, [CLIAC MEMBER], you had your hand up first. I'll ask you first.

CLIAC MEMBER: I just have a little concern about the educational requirements. Because as I was reading through them, how does one even become a bioinformatician because we are requiring that they have two years of training before they even start? So how do they even get their foot through the door, then? We would never be able to hire anybody unless they were already working in a lab, I guess, unless I'm understanding that wrong.

DR. NIRALI PATEL: Yeah. So that is a-- that is a very fair definition. And I think the idea of that was, again, to be working in a laboratory environment without primary responsibility for high-complexity without having that primary responsibility for generation and oversight of that bioinformatics data. So I think one of the examples of I think how we qualify moderate to high-complexity personnel currently are they may be in ancillary sort of support type roles. They may be in your specimen processing or returns, work in a moderate complexity area of the laboratory before they're given that final responsibility for data analysis in the bioinformatics purview. And so-- yeah, we did not we did not exactly define what those sort of preroles would be before you qualified as the final personnel. So I do think that was probably something of an oversight on our end with more of the spirit.

CLIAC CHAIR: Reflect back, though. It's not necessarily two years of bioinformatics work. It's two years of laboratory work.

DR. NIRALI PATEL: Yes.

CLIAC MEMBER: But you're also saying a genetic counselor could do it. So you would make a genetic counselor be a phlebotomist or something for two years before they could participate in the bioinformatics part of it? I don't see that happening. I mean, if you go after a master's in mathematics person, and you tell them that they're not going to be able to perform their function as a bioinformatics person until they've completed two years of wet lab, which they will not be in any way appropriate for, the only thing they could do really is LSS, laboratory support, or phlebotomy because you would want a clinical laboratory scientist for actual-- I'm just worried about the unintended consequences that we have raised the bar so high that there will be actually few people who will be able to do this.

CLIAC CHAIR: And to be clear, what I'm hearing is to potentially loosen the requirement for that entry level bioinformatician.

CLIAC MEMBER: Yeah,

CLIAC CHAIR: Yeah. So I wrote it down. I think that's more of the details part. We will absolutely get to it. I want to see if there's any conversation related to the spirit of it. What I'm hearing is you support the spirit. You just see a potential problem that may we need to resolve. [CLIAC MEMBER]?

CLIAC MEMBER: Thanks. I have problems with the educational requirements, too, because it leaves out different routes. We offer this at the University of Iowa to a degree in epidemiology. Someone with an epidemiology background has a lot of data and analysis, and we're not including them in this group. But I'm also not sure what we're trying to get at here because there's commercial sources for analysis as well. We use a provider called BugSeq that we can send data to their pipeline and get the analysis back, and they have experts. Do I have to meet the CLIA requirements and make sure that those folks are meeting these same qualifications? Because I agree with [CLIAC MEMBER] that we're not going to be able to hire people. There's not enough bioinformaticians to go around. And it's a really important tool for epidemiologists. I also question-- this is used basically for surveillance activities. It's not used for public for treatment as such, except if you're looking at the case if you're looking for a gene or some treatment for cancer treatment. Can we better define when this is important and when it's not? Because I don't think it's important in all situations.

DR. NIRALI PATEL: Yeah, as far as the remit of when a sort of licensed bioinformatician would be considered testing personnel, from your comment about when you're using these data analysis tools that are used for surveillance and aggregation of results, we would consider that outside of that, intended for use to treat a patient with a clinical test result. So that would not need a CLIA bioinformatician role to do that. But there is-- you did bring up the idea of external software. And there is currently a concern that external software, again, is one component of a multifactorial tool. If you do slightly different wet lab processes, you can have the same bioinformatics pipeline yield different results because that bioinformatics pipeline is not calibrated to your wet lab input. And so as a clinical laboratory, you do need staff within your testing pipeline that can assess those vulnerabilities in that externally packaged software before you qualify it as part of your testing system.

CLIAC MEMBER: I agree. Thanks

CLIAC CHAIR: Thank you. And I also see [CLIAC DFO] putting something up here to show.

CLIAC DFO: I can't raise my hand, I guess, because I'm a host. But I want to-- this is in our workgroup report. I want to remind everybody that there are new testing personnel qualifications that are effective at the end of this year. This is all the new ways that you can qualify as testing high-complexity personnel. We've included this as Appendix B in our workgroup. Penny Keller from CMS came and gave a wonderful presentation to the workgroup on this final rule and the new requirements for testing personnel on how to qualify. So we're not saying that you can't still qualify under here. We're just saying if you qualify as an epidemiologist, which would be a biological science degree, you can still qualify that way. You would just need two years. And there was much debate about the two years, but you would need two years of experience working in a laboratory, performing some type of bioinformatics data analysis. So I want to point out that if you do not have any of these degrees and you're just going on semester hour requirements, similar to what we did, you still have to have three months of documented laboratory training in each specialty where you are performing high-complexity testing. So these are the new requirements if you don't have a degree and you want to meet this, what we're calling "educational pathway" that we have developed in the personnel final rule that will be effective at the end of the year. So we used this as the basis for the personnel requirements that were developed. So we're not saying that, oh, you have a biological science degree, you're not able to do bioinformatics data analysis. It was just you can still qualify all these methods, but you also need additional training. So just look in the workgroup report, Appendix B. and it's there if you have any additional questions about what that means.

CLIAC CHAIR: And I'll also share for the group how envisioning these recommendations moving forward is that we'll have those high-level recommendations that are bullets 1 through 4 on the report. I'm sure [CLIAC DFO] could pull it up in a little bit. And then the details that the workgroup diligently worked on in terms of describing what the responsibilities are, as well as the educational requirements, those would be sub-bullets under the recommendations, requesting that CMS consider these as components of it. So I'm trying to relieve a little bit of the burden of us getting it perfect. Obviously, if we have time just to really spend on it and try and make it closer to perfect, that's fine. But perfection is not what we're needed here. We need the recommendation to state what we want it state. It also gives the agency the flexibility to compare what we're putting forward to existing educational requirements so it fits more cleanly into a bigger picture of educational requirements. We're not painting them into a corner. [CLIAC MEMBER]?

CLIAC MEMBER: Thank you, Nirali and team, for putting this. So I essentially agree with the spirit of the workgroup. I think this is really great and we need to acknowledge and somehow add them to the CLIA. They work already. We already have all these bioinformaticians in the lab. Maybe codifying how we select them, I think, is an important thing. We can always discuss the specifics of the definition. But when I'm looking at the bioinformatician definition, the first one is actually in my bioinformatician because as [CLIAC MEMBER] say, we have packages I can manage, process, analyze biological data, utilizing specialized software. I'm wondering if part of what we want to highlight is that these people have very special skill. They can write, they can write some of these code. They can develop those pipeline. Do we want to make it a little bit clearer, or do we just want to open it? Because I think this can clarify a lot of people to just be bioinformatician and get in the lab, as opposed to maybe that very specialized skill set that we want to make sure those people have to qualify and declare under this new route that we're writing through.

DR. NIRALI PATEL: Yeah, I know.

CLIAC MEMBER: Right.

DR. NIRALI PATEL: And that's exactly-- I think we spent an hour on actually, I think, one of these definitions, where we started listing about 20 different core components. And then we realized that each of those core components did sort of roll up into this more generalized description. And again, I think a lot of what we came back to is that even under our current CLIA personnel testing requirements, we are relatively general that the technologists are performing procedures involved in laboratory testing. We're not saying the pipetting or the mass spec. And again, even though there might be common actions between, let's say, the microbiology discipline and the molecular discipline, when you're in that high-complexity testing, it, again, falls under that sort of lab director purview to say OK, you are my microbiology staff, yes, you were in that discipline, versus here's my bioinformatics-targeted staff that may be doing that. But again, definitely something that we may want to expand on.

CLIAC MEMBER: And the document you were sharing earlier, [CLIAC DFO], I think the personnel requirement, I think the first few lines have information about license. This group of people don't have license or board certification. Would that need to be changed because it's licensed and all of these other requirements? Or licenses, just something--

DR. NIRALI PATEL: So since there weren't any CMS, HHS-approved certification pathways for this-- and that is actually something the field is working on-- that's why we focused more on those, again, primary scientific course requirements because we couldn't require a certification that does not currently exist.

CLIAC DFO: And I will clarify in that Appendix B. Those are all the routes. You don't have to meet every single one of those qualifications. Those are just the routes to qualify as testing personnel.

CLIAC MEMBER: I was just making sure because it seems like the first paragraph lists the license and then the different routes. So it's not the license and one of these routes, it's completely independent? OK, good. Thank you.

CLIAC CHAIR: Excellent. Before we go on to the next question, I did want to just state I forgot to mention that we do not have any public comments, so that's why we skipped over that section. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: Getting off mute here. Thank you so much for this really wonderful and hard work. This is something that really needs to get called out. Interestingly, in the last month, I have had five students approach me asking me how to get into bioinformatics, what is bioinformatics, what would they do when they grow up. And so young people are really interested in this. And I think it's really important for us to define this so that they know what the expectations are. This helps people get into the field. I support the spirit. I think the details are a little bit tangled up, and I think we need to work on it. But I want to go back to a really important detail, and this is going to be subtle. But informaticists do not refer to ourselves as informaticians. We learned a long time ago that that sounds like a mortician or a beautician. And so I would like to suggest in a friendly amendment that we use the term that's used by the American Medical Informatics Association and the Pathology Informatics Association and use the word "informaticist," not informatician. I know that's a little bit subtle, but I think it's really important. And I'm thinking of all my senior colleagues that are rolling over either in their graves or in their beds right now hearing that term be thrown around. So I hope you find that friendly, Nirali, but I really think it's important to call that out. In fact, I went and I grabbed the textbooks just to make sure I wasn't making this up in my own mind. And there's several discussions in both the AMA's books and Shortliffe in the pathology informatics text. I think it's really interesting as well to look at the qualifications because there's a lot of different aspects to this. And one of the things that I didn't hear really get called out was the idea of this in-lab experience being considered to be what we often refer to as an internship. This is the way we do it with medical laboratory scientists, clinical laboratory scientists. They have to have a component of that training that's within the laboratory. And typically that's considered to be some sort of a formal internship. So I'd like to suggest that we somehow get that word in there. And then to I think it was [CLIAC MEMBER] point, when we talk about bioinformatics, we're really talking about molecular diagnostics and molecular laboratory. It's just not data from biological systems. In fact, your definition of bioinformaticist could be image analysis.

And I think we need to be a little bit clearer about that because bioinformaticists are focused on DNA, RNA, protein-oriented work. It's not just any biological system. Otherwise, how would you separate them from computational pathologist, image analysis technicians, so forth and so on? So I'd like to see more flavor orienting this towards the molecular diagnostic pathway and how it relates to the clinical laboratory. That's about all I can squeeze out in a logical comment to this, Nirali. There's so much baked into this. I literally feel like I want to go chew on it for the rest of the evening and come back with something more intelligent.

DR. NIRALI PATEL: Thank you for that. And I will say, especially since you bring up image analysis, again, there are starting to be multifactorial models being proposed for clinical testing that integrate not only the genomic and transcriptomic data but also utilize some image-based analyzes. And again, each of these are clinical lab specimens. And we got yesterday bioinformatics is primarily focused on that molecular and sequencing data. I again think that part of our discussion was we don't necessarily know what technologies or techniques or components of that-- let's say microbiome may be coming next, which is why we did go for more of this expansive definition.

CLIAC CHAIR: Yeah, it's the age-old conversation of detail versus broad. And I can share my personal belief is, especially as we're talking about regs and standards to be as broad as possible, recognizing to your point, [CLIAC MEMBER], that the risks are being overly inclusive. It's just threading the needle of where we're comfortable.

CLIAC MEMBER: And Nirali, do you accept my friendly amendment to use the term "informaticist" not informatician? I think that's the most important point I wanted to make.

DR. NIRALI PATEL: I would say we had a group of, I think it was, 25 folks who are in the bioinformatics sphere, and they all aligned on bioinformatician for this.

CLIAC DFO: So I will want to preempt that it was with the scope of this or CLIA. So a lot of the informatic practices that were discussed were the practice of medicine. And felt strongly that the language of informaticist or informatician was outside of the scope of the laboratory testing process. And that's why they landed on bioinformatician.

CLIAC CHAIR: Yeah, thank you. [CLIAC MEMBER]?

CLIAC MEMBER: I listened to the prior two questions and discussion with great interest and I would also say perplexity because the word that keeps coming to my mind is profession. You are defining a new profession, which is a term that's a statutory term in the state of New York because if there's a license attached to it, it's a profession. Right now, I'm not aware of bioinformatics requiring licensure. And to have your preface reference the possibility of a license being required, that is definitionally a medical laboratory scientist or some other professional positions. So that I worry about the job that you are describing, the statement of work that you're describing, not actually being a profession but instead being a set of requirements for someone to be able to perform testing, which is my second point, part of the same point. Is the performance of bioinformatics the performance of laboratory testing? Because if it is, then you have a profession, in which case there's a whole logical sequence not of qualifications but of actually saying this is a specific professional position which is or is not that of medical laboratory scientist or a professional degree, which is my concern for-- The spirit is spectacular. I think this is exactly what we need to be addressing. And I applaud the effort that's been put into it. My concern is it risks foundering on what's the performance of a laboratory test and what constitutes a profession.

CLIAC CHAIR: Yeah, those are good points. Nirali, remind me. Was there-- because I didn't catch that. Was there a licensure?

DR. NIRALI PATEL: So there is no licensure requirement here because, again, there is no established licensing board or certification in bioinformatics that is sort of globally present at this time. And to the point where, again, making them part of the laboratory testing personnel, I think one of the things that came up very frequently from the lab directors was that you can't report out these results without this staff. But the way CLIA is currently set up, you can't necessarily even acknowledge them as part of your critical laboratory team. And I think that really sets up an intrinsic sort of disconnect occasionally with management or financials, where, again, you're not able to fully bring these personnel into your requirements for regulatory compliance. Because, again, yes, my bioinformatics people are core to me resulting out this test, but they also don't fall under the purview of clinical laboratory personnel. So are they waived from the competency and proficiency requirements? And so I think it's sort of that push-pull between we need them to report out a clinical result, but we also cannot acknowledge their explicit role in the laboratory, which is why we wanted to define a pathway to really pull them under this testing personnel umbrella so we could really define for anyone on the outside looking in how this critical workforce is truly an intrinsic part of the laboratory and not an optional component for this high-complexity testing.

CLIAC MEMBER: And is there a way to translate what you just said into a CLIAC recommendation? Other than you have the qualifications, but you're actually making a more global philosophical statement about this constituting a professional workforce that's under the laboratory umbrella. And to me, the safe landing zone is it's under the medical directorship of

someone above them. So that could be—[CLIAC CHAIR], I do hear the shaping of a recommendation as to the intent of what's happening here. And I think Nirali has articulated the need for that shaping very nicely. Because it's not clear in the prologue to the text that's on the screen here.

CLIAC CHAIR: OK. [FDA EX OFFICIO]?

FDA EX OFFICIO: Yeah, thank you. So I had a question. I think I understand that some of the proposal relates to identifying these individuals as someone who would use, perhaps select, put together bioinformatics pipeline, troubleshoot, et cetera. But I see in the Responsibility section you talk about "develop and modify." What did you mean by that?

DR. NIRALI PATEL: So by the "develop and modify," again, when you first implement a pipeline in clinical testing, if you need to, let's say, add on a specimen type, that exact same analysis software may not be able to-- let's say in the DNA or RNA space-- may not be able to appropriately identify the same artifacts. And so in order to potentially add on a specimen type from the wet lab process, you may need to add additional parameters to that data analysis to allow for, again, those pertinent true positives to be identified, just because of the wet lab differences between those specimen types. That's what we were saying when we were talking about modifying as applicable. Also a good example is when human genome builds get updated. You get better mapping of DNA fragments and more accurate variant calling. And so in order for your test to be able to incorporate that new human genome build, you would have to modify your pipeline to take in that additional data to allow you to generate that more accurate result on the end.

FDA EX OFFICIO: I'm not aware that CLIA regulates software development and design. And so I think that we need to draw a line between the use of a medical device software and the development of software, which has typically been a medical device development design activity and not really a CLIA activity. So I don't know if you have reactions to that, but if you have a software program that has parameters that you set and use, that's kind of more of the use of the software program. But if you're developing the software yourself or going into code, that might be more of a software design and development activity, which I'm not certain would be under CLIA. So we should define, I think, this as something well within CLIA's purview. So that's probably my recommendation.

CLIAC CHAIR: Yeah, it's a good point. And especially-- again, we're getting into thin ice here. But I absolutely hear what you're saying. And particularly the word "develop" is the reaction. So, yeah, I think maybe some wordsmithing there could probably alleviate that, even potentially as simple as getting rid of the word "develop."

FDA EX OFFICIO: Maybe "modify" also, depending on how we're using that. Thank you.

CLIAC CHAIR: Yeah, right. I guess in my mind I was using "modify" as the tinkering with the parameters, like your example that you gave. But yeah, that's probably not a modification. Modification sounds like code modifying.
OK, we had [CLIAC MEMBER] then [CLIAC MEMBER], and then I want to start to transition to shaping out the recommendations.

CLIAC MEMBER: I have deep angst with this, mainly because I have the fear that we are going to set up laboratories to be at a disadvantage for a very limited resource. And so I guess-- I think I work best when I use case studies. So if I am setting up a panel and I want to use bioinformatics pipeline, I can either use an in-house resource or, as someone alluded to earlier, I can also go third-party. I guess my fear that we're setting up here is that if I choose to go with a third party who purely does data analysis and does not perform patient testing or anything like that, they will not be in any way encumbered by any of these requirements. They have in-house staff who perform bioinformatics processing and analysis, but they are purely a software shop or analysis shop. And I can use them, and then I determine the panel that I want off of their data. If I choose, however, to try and bring that resource in-house, I basically have to hire somebody who either has already two years experience or somebody who's fresh out. But then I have to have them work in the lab in a different function than what it is that I'm hiring them for before they can serve me as a bioinformatician. I want to make sure that we are not setting up labs for failure because we are hamstringing them and pretty much forcing them to use outside, third-party options, which we might not even know the quality of, basically, and which I don't think CLIA would be extended to.

CLIAC CHAIR: I wonder if with this-- and I'm just thinking out loud-- if with this referencing a part out-- and I want to make clear because I've heard two flavors of that referencing work out-- referencing that work out as part of the analytical process and referencing that work out as development process. I don't know if we should consider this to be the scope. We're defining what the CLIA requirements are for an in-house bioinformatician. I don't know if we are prepared, if we were thinking of the inclusion of external folks falling under this. Nirali, what are your thoughts on that?

DR. NIRALI PATEL: Yeah, so there was some conversation about, again, there are external software companies that do provide this as a standalone service. And currently to that point, they are sort of outside of the regulatory authority of CLIA because, again, bioinformatics itself as a discipline isn't really within the purview of CLIA. And so, again, even if you have

one of these external vendors, when you have an external vendor, currently the responsibility for assessing and maintaining it really rolls up under the laboratory director in CLIA. Because even if you do employ a bioinformatician, you can't qualify them in any way, shape, or form as testing personnel. So that is truly sort of outside of the visibility of CLIA, which is, I think, what was one of the main concerns. Because there is this entire segment of the actual processing of the specimen, which is how the data is analyzed and generates that result, that is currently outside of the purview of CLIA. And so I think what we were trying to do, again, is bring in that personnel. And again, that does still-- to, I think, [CLIAC MEMBER] point-- not address the potential application of these outside vendors. And I don't know if that's potentially a secondary workgroup analysis. Because we really were focusing in on how do we actually get these folks to be more explicitly part of our laboratory testing personnel. Because that is a function they're doing today, and that's going sort of unrecognized and just undeclared in our current oversight.

CLIAC CHAIR: So reflecting back what I'm hearing, again, I think you're validating the scope comment. Is that where--

DR. NIRALI PATEL: Yeah.

CLIAC CHAIR: --this is referring to in-house hires of bioinformaticians.

DR. NIRALI PATEL: Yes.

CLIAC CHAIR: So we have 23 minutes left. [CLIAC MEMBER] and then [CLIAC MEMBER], I'm going to get to you in a second, although I don't know how [CLIAC MEMBER] jumped over [CLIAC MEMBER]. I thought [CLIAC MEMBER] was next. But give me a second. [CLIAC DFO], while we're going through [CLIAC MEMBER] and [CLIAC MEMBER], could you put up the four recommendations? And could you also put, if you can, the sub-bullets of what the educational requirements are and the qualifications are as sub bullets under those, the appropriate of the four recommendations? Because I want to create the framework that we're approving the four bulleted recommendations. The additional information in terms of the qualifications and requirements are context that we're providing to the agency to use, but we are not restricting them to it. And then I would like to maybe add some additional comments there. First, as just a placeholder, I would love to say that we want to, for, say, the qualifications as a qualifying statement, to make sure that-- consider loosening them so that we don't have an a burdensome barrier for entry-level positions. And if we have time, we could then maybe flesh that out. But at least it's there, or we could approve it. So while you're working on that, [CLIAC MEMBER], did you take your hand down and then back up?

CLIAC MEMBER: I didn't realize it. I had unmuted myself so that I wouldn't have to unmute myself. And every time somebody finished talking, it took the hand down. [INTERPOSING VOICES] Yes, it's been going up. OK, so I just want to introduce a little bit of humor. This has been a huge amount of work, and it's a tremendous problem. And it reminds me of the Supreme Court Justice, Potter Stewart, who commented that he could not define pornography but he knew it when he saw it. [LAUGHTER] So on a serious note, I don't have the people who are involved in front of me right now. Was there anybody from a health professions school? Because I do know at MD Anderson, Professor Peter Hu in their health professions school teaches-- well, he leads people in doing PhDs in molecular biology but specifically so that they can work in a health professions laboratory. And it might be interesting to get their purview. As for the experience, I wonder if some of a PhD or master's research project could qualify as experience. I wonder in terms of those educational requirements, are they fixed? There was a comment in the chat also saying maybe they should be made more general. And if not, I would definitely include statistical genetics as an area that does that. You might find it easier to go from a list of what they should be able to do and then go backwards to how they've been trained because I think they do have to be able to develop a proficiency testing plan for software. And then finally, I want to say that modification of software is really a can of worms. You can modify software, and it'll break something someplace else, and you won't know for six months. And that's quite different from modifying the inputs or changing some of the parameters that put weight on one thing more than another that are adjustable parameters that you can adjust, or the library that you can call on. So I would make a modification of the algorithm something that would require testing. And would that be like an LDT-type testing situation, where it is more like in vitro diagnostics? And then finally, although it is a different type of software, I'm curious as to where the FDA and where HHS in general and CLIA is going on AI testing. I think that's done by the FDA. So would this fall under the FDA? But I definitely think there should be a list of what this person should be able to do. Should they be able to code? Should they be able to develop a proficiency testing plan? Should they be able to update the software? Should they be able to update the libraries that are utilized by the software? And then again, Peter Hu's a great guy. I can put you in touch with him to give you some background on what their education requirements are before they send people out.

DR. NIRALI PATEL: Yeah, no. And again, I think your comment on the genetics background-- and to [CLIAC DFO]-- I don't know if genetics, for example, would fall under biology. And again, because the previous CLIA testing personnel disciplines were considered in scope. So I don't know if statistical genetics as a specific thing falls under more of a biological science or a computational science. But yeah.

CLIAC MEMBER: Yeah, I think actually, I've seen it as a PhD. I have a PhD in statistical genetics, the title is. So there are departments of statistical genetics. They may be under math or bio or a department of their own that's in between.

CLIAC CHAIR: Yeah. And just to call out-- we're never going to get all the different titles-- not titles-- all the different--

CLIAC MEMBER: No. So you might want to be a little more general and say relevant areas of the biological and data sciences that would include examples such as these.

CLIAC CHAIR: Yeah, agreed, recognizing it'll never be all-inclusive. There's no real standardized nomenclature of what to call these degrees. So it will have to be as-- we need to get it to "good." We'll never get it to "perfect." [CLIAC MEMBER]?

CLIAC MEMBER: My comment was just on the data. Yeah, the data. And data is not a specimen, somebody said. But in our last CLIA workgroup, we actually discussed AI and machine learning and all that. And because it was part of a patient's specimen interpretation, it was sort of all-inclusive. So I do think it is important to bring that fact that you're providing a patient result in some way for these people who may have a mathematical background but are going to ultimately be doing that interpretation medically, so there has to be some kind of connection. But the data-- my understanding was data is part of the specimen. I think it was-- who was-- somebody put a comment in. And I fully agree.

CMS EX OFFICIO: That's me. Data is not a specimen. That's going to be a huge, huge issue. It's something CLIA can definitely attack someday if you want. But if data was a specimen, then that would pull all the 23andMe under CLIA. That's not something that we're real comfortable with taking right now.

CLIAC MEMBER: But [CLIAC DFO], clarify for me because I may be completely misunderstanding what our last workgroup was, and that's what we were talking about.

CLIAC DFO: There is a workgroup. There is a CLIAC recommendation that the definition of a laboratory should be updated to include data.

CLIAC MEMBER: Yeah.

CLIAC DFO: So that would have to be moved forward in rule-making, and that's something that we are not addressing at the moment.

CLIAC MEMBER: OK, OK.

CLIAC CHAIR: I think that this differential here being that was the recommendation, but it is not in the regs.

CLIAC MEMBER: No, no, no, I know, but I think it's just because it's something pending. So I think we need to think about it anyway. All right.

CLIAC CHAIR: OK, [CLIAC DFO], I see you put that statement on the bottom, the information to agencies to be used, should rule-making proceed. Are you there going to put in all of those qualifications and things like that? OK. So yeah. So. we have 15 minutes left. And what we need to agree upon is the recommendations, which are these four bullets. All the other information that we have then subsequently debated and refined is going to fall into that information that the agency should consider. We're not telling them to do this. They have to consider it in a much broader context. And certainly we can provide that guidance. I think what the group put forward is a really good-- I don't even want to call it a first draft because I think that underplays how much work was done into it. And I think that our comments, I think we could add to it as other bullets. Could be very useful information for the agencies. So certainly yeah, like I said, Heather, if you can copy and paste those qualifications or responsibilities, that'd be great. I think a statement stating to caution the agency to make sure that these requirements are not overly burdensome for entry level positions. That's something I heard the group say. Up to and including-- the term that was used was "internship." I think that's another something that can be considered as part of that to be able to get them into that entry-level position with real experience, not just academic classroom experience. And to be honest, I think a lot of the other conversations we had were really good. But I think we're just outside the scope of what we were trying to do here is define what a bioinformatician is in the laboratory. Worthy conversations. I think maybe discussions we can have in the future, but I think slightly out of scope of what we were trying to do here. So with that-- and I see a couple of hands up-- but with that, I wanted to go through the four bullets one by one to see if there was any significant disagreements-- again, not wordsmithing, but significant disagreements of the spirit of it. So, again, bullet number 1 is to really define what a bioinformatician is, leveraging the carve-out that was as precedent used for blood gas analysis. Any problems or issues with that recommendation? So, [CLIAC MEMBER], I see your hand, but I don't know if it's a comment or if you have an issue with that.

CLIAC MEMBER: No issue with that bullet point specifically, but I do have-- and maybe I'm just showing my lack of experience here, but the workgroup and the title of this document had something to do with next generation sequencing. And then we immediately move into bioinformatics, not mentioning next generation sequencing. So what is the tie there? I'm kind of lost.

CLIAC CHAIR: Yeah, Nirali, you want to do as you wish?

DR. NIRALI PATEL: Yeah. So the next generation sequencing was the larger remit. And then as part of that, a subcategory was the need for bioinformatics personnel. So this is one component of that larger NGS initiative.

CLIAC MEMBER: OK, that sort of makes sense. But I think the laboratory and laboratory medicine is moving in this direction, regardless of whether it's next generation sequencing or whatever it is. Bioinformatics is becoming a thing, and that's good. And maybe we need to define it and add some structure to it. But I'm not sure that I get the reason why next generation sequencing has produced this.

CLIAC DFO: So the CLIAC recommendation was based on next generation sequencing and the role of bioinformaticians in doing that bioinformatic pipeline portion of NGS. And we had a CLIAC workgroup which [CLIAC CHAIR] was the chair of that reported back in April 2019 that made this recommendation. And then there was a subsequent NGS-specific CLIAC topic that said there should be a workgroup forum to discuss how laboratories can qualify somebody who's performing that bioinformatic pipeline analysis piece of these tests. And so that's where this workgroup was formed out of. The discussions in the workgroup basically came to the consensus that you just said, that it's not just NGS. There's a lot of other processes out there that are utilizing these bioinformatic processes and data analysis. And so that's why NGS was kept out of it and kept it a little bit more general in their discussion points.

CLIAC MEMBER: OK, good. That's helpful. But then why leave next generation sequencing at the top of these documents or whatever we're going to produce here, these recommendations?

CLIAC DFO: It's a formality. So with any CLIAC workgroup, we have to get a formal terms of engagement and everything approved by the FACA committees here at CDC and HHS. And at the time, it was called the Next Generation Sequencing workgroup. So that's part of it. But bioinformatics and bioinformatics pipeline development is a massive part of any NGS test process.

CLIAC CHAIR: OK, thank you. So any-- again, any I'm not hearing any spiritual conflicts with bullet number 1. How about number 2? So again, to summarize-- and [CLIAC DFO] and I could work in terms of putting these into recommendations. CLIA recommends blah, blah, blah. But we're looking for spiritual alignment here. So the second bullet is saying just to basically leverage the existing personnel roles of testing personnel, general supervisor, et cetera, and to apply that framework to bioinformaticians in the CLIA environment with both that tiered responsibility as well as the tiered requirements. Any issues there? [CLIAC MEMBER]?

CLIAC MEMBER: Yeah, thanks. So just kind of hearken back on what [CLIAC MEMBER] and [CLIAC MEMBER] had mentioned at the very beginning of this, and hoping this is the right bullet to bring this up again. With regards to the education requirements I think OK. But the experience requirements, again, considering that there are no, at least that I am aware of, training programs specific to bioinformatics, unlike medical technologists or CLS, clinical laboratory sciences, that sort of thing. So we talked about underneath there in the sub-bullet about internships. And I would also add, by the way, Heather, fellowships in addition to internships-- excuse me-- for a two-year experience requirement. But I am a bit concerned about that, and I know we've talked about that to an extent here. Curious to see, again, whether or not this needs to be discussed and this is going to be finalized with the amount of experience that's required and whether or not that's going to be above and beyond minimum requirements currently for other testing personnel. Again, even if so, I bring up the fact that there are no training programs. We talked about surveillance versus non surveillance, clinical testing. Could somebody who was working in-- again, clarifying question for the working group. But in a surveillance atmosphere with that experience, does that count towards now if they want to move over to the clinical side, does that count? So there's lots of questions here that I think remain unanswered. Thanks.

DR. NIRALI PATEL: Sorry, friendly amendment. And to that point, again, information that agencies should consider. Internships and fellowships should be considered as part of an experience requirement with length to be determined. Because again, to your point, yes, we did say two years because that's what we've sort of seen the way we've sort of ad hoc done it in our laboratories to date. But if we are seeing that we are getting more opportunities, again, like with those structured opportunities, could those be shorter. So yeah, I wonder if rather than just in this top set of bullet points putting those explicit years, saying yes, this is part of that consideration.

CLIAC MEMBER: And by fellowship, are you including a postdoctoral fellowship? Postdoctoral training? If you have a PhD and you do a postdoctoral training and you're analyzing this kind of data.

CLIAC MEMBER: Or even master's level.

CLIAC MEMBER: Or master's level.

CLIAC MEMBER: Yeah, sure, yeah. [INTERPOSING VOICES]

CLIAC MEMBER: --thesis projects that covered this kind of analysis.

CLIAC CHAIR: We're getting into the world of being overly prescriptive. Overly prescriptive is not helpful for regs. I think the spirit here is that you have real-life laboratory experience in some way, shape, or form.

CLIAC MEMBER: Yeah, I think that sounds good. Actually, just that phrase exactly.

CLIAC MEMBER: So laboratory experience. That's what we do in the lab. The clinical labs now.

CLIAC CHAIR: Exactly.

CLIAC MEMBER: You don't take a person that graduates and put them at the blood bench. They work for a year in that setting.

CLIAC CHAIR: Yeah. I mean, experience can be defined-- within reason, is defined and accepted by the lab director.

CLIAC DFO: And then I'll just remind everybody. Any type of rule-making that occurs, should this move forward, as you all know, you will put out a proposed rule. We just went through with PT, and we just went through it with personnel. Should this move forward in any way, shape, or form as a rule-making process, there is a proposed rule that goes out. And there are public comment periods. For instance, in the personnel proposed rule, as you saw in the final rule, when we do our comment analysis, there were multitudes of individuals and professional organizations that provided comments and feedback on those proposed changes. And the agencies do have to respond to the comments received and justify why we are keeping the regulations as is or why we are changing them. So CLIAC can suggest high-level recommendations like this. But anything that moves forward, there's ample opportunity to provide feedback and comments yet again.

CLIAC CHAIR: Exactly. We are providing a recommendation and a general framework of which the agencies can chew on, with several rounds of public comments. Maybe not several rounds, but there are rounds of public comments to refine. So we have these two recommendations. It's kind of the consolidation of the overall four. I'd like everyone to take a minute or so to just read them, recognizing that we have the qualification statement underneath, that is, the information about agencies. And I'm going to ask you to take a minute, read it. And I'm going to ask if we could move forward with these recommendations, again, appreciating that there's more rounds of input on the back end of this. It's funny. I'm looking at people's eyes to see when they stop darting across the screen of when I can take questions. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I'm wondering about the word "additional" in the second line because are we not trying to clarify responsibilities? "Additional" is just an odd word which seems a little unnecessary. A qualification route for the responsibilities of bioinformaticians. You could say it's wordsmithing, but my primary concern is about the word "additional."

CLIAC CHAIR: Fair enough.

CLIAC MEMBER: So, [CLIAC DFO], for the responsibilities of bioinformaticians. I think that's the spirit of what we're trying to get at. And then, by the way, that single top line answers my concern about are we creating a profession. Keep it simple.

CLIAC CHAIR: Yeah, exactly. OK, so it seems like everyone's had time. I see no other hands raised. I would ask, do we have a motion to approve these two recommendations, with the caveats of the sub-bullet-- the additional information of the sub-bullets as well as the caveats at the bottom of the screen?

CLIAC MEMBER: I'll move.

CLIAC CHAIR: Sorry?

CLIAC MEMBER: I said I move.

CLIAC CHAIR: OK. Do we have a second?

CLIAC MEMBER: Second.

CLIAC CHAIR: Thank you. OK, let's go to a vote. All in favor, please raise your virtual hand. OK, it looks like we have a majority, so these will pass. Excellent. So with that, we have concluded day one precisely on time. So I do want to thank you for joining this CLIAC meeting. We obviously have a second day tomorrow, which will begin promptly at 11:00 AM Eastern Standard Time-- or Eastern Daylight Savings Time? And just as a little teaser, our topics for tomorrow are going to be all brand new topics for us, focusing on cybersecurity requirements in the clinical laboratory, proficiency testing, determination of clinically relevant range of values, and finally, the utilization of remote technology for competency assessments. So again, I thank you very much for your day today. Have a great night, and we'll see you all tomorrow.

CLIAC MEMBER: Thanks, Jordan.

CLIAC CHAIR: Thank you.

CLIAC MEMBER: Thank you, everyone.

November 7, 2024

❖ Call to Order

CLIAC DFO: Let me start the recording real quick. So again, my name is Heather Stang. I am the Senior Advisor for Clinical Laboratories in the Division of Laboratory Systems and the Office of Laboratory Systems and Response at CDC. I also serve as the Designated Federal Officer or DFO of CLIAC. CLIAC is managed by the CDC and provides scientific and technical advice and guidance to the Department of Health and Human Services. This advice and guidance that CLIAC provides to HHS focuses on issues related to improvement in clinical laboratory quality, laboratory medicine. Also, in addition, the committee provides advice and guidance on specific questions related to possible revisions of the CLIA standards. As this is a federal advisory committee meeting, the Zoom chat and Q&A functions have been disabled for online audience members. You are listen only mode if you are an audience member. So if you are experiencing Zoom difficulties, please contact cliac@cdc.gov. Members are reminded of the importance of remaining in attendance for the full meeting to ensure a quorum until all matters before the committee are addressed, and the meeting is adjourned. We will not be doing an official roll call this morning. If audience members would like to find out more information about our CLIAC members, please visit our CLIAC meeting website. Thank you, and I will turn it over to Jordan.

CLIAC CHAIR: Excellent. Thank you, Heather. Just as a reminder of some of the operations and logistics of the meeting, during the period dedicated to the committee discussion, participation is limited to CLIAC members only. CLIAC can only accept public comments that are directly related to the topics announced in the Federal Register Notice announcement of the CLIAC meeting. Today the committee will discuss and deliberate on cybersecurity requirements in the clinical laboratory, proficiency testing, determination of clinically relevant range of values, and utilization of remote technology for competency assessments. Public comment periods are scheduled at the end of the presentations. If anyone in the audience wishes to address the committee, the public comment portion of this meeting is the proper forum to do so. If you wish to provide a five minute public comment on any of the topics discussed today, please email cliac@cdc.gov as soon as possible for inclusion in the public comment period. Get a little bit about logistics, copies of the PowerPoint presentations and other meeting materials are posted on the website. This meeting is being webcast via Zoom webinar, and we welcome everyone online today. Links to access the webinar are provided on the CLIAC website. The meeting is also recorded in order to assist in preparing an accurate written summary of the proceedings, as well. So we could roll right into it.

Today, we will start with our cybersecurity requirements and the clinical laboratory. We'll start with an introduction by Mr. Gregg Brandush, the director of the Division of Clinical Laboratory Improvement and Quality at CMS, followed by a presentation on cybersecurity considerations for clinical laboratories by Dr. David McClintock. Dr. McClintock is the chair of the Division of computational pathology of AI in the Department of Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota. After the presentations, we'll have time for committee discussions, as well as public comments. So with that, I will turn it over to Gregg.

❖ Presentations and Committee Discussion

Cybersecurity Requirements in the Clinical Laboratory

Introduction to Topic
Gregg S. Brandush, RN, JD, CMS Ex Officio

MR. GREGG BRANDUSH: Thank you, Jordan. I'm just going to give a brief overview of cybersecurity, lay the groundwork for the problem, go over the existing regulatory structure, and then have some items for discussion. So the scope of the issue, and this comes from the two links you could barely see at the bottom there, the Health Care Finance News and Health Care Guy, I believe, dot com. Ransomware attacks accounted for 70% of the successful cyber attacks on health care organizations. Over the course of nine months in 2023, more than 1,600 health care organizations were affected. And that each of these cyber attacks cost an average of $11 million per breach. Within the health care industry, more than 1 in 4 ransomware attacks affects patient care. Half of the organizations that suffered an attack said patient data was compromised, and more than one third of health care companies reported not having a cybersecurity response plan, which is pretty alarming, given the degree that we're all aware of this issue. And there's really two issues. So there's one. Any health care organization has an electronic record system. That data system gets attacked. It's not available. It's compromised. So that is going to adversely impact care. And then the second liability on the part of that agency is lawsuits. People get very upset when their personal health information is compromised. So they have to exert resources in order to protect and defend themselves on that front. So the current cybersecurity regulations in CLIAC-- and I thought this would be a good groundwork so everyone has the same level of understanding. And it's interesting to note, the word cybersecurity doesn't apply anywhere in any of this. It's more really broad, in general.

So the first is 1251B14. This refers to the procedure manual, and it identifies what must be included in the applicable test procedure, so a description of the course of action to take if a test system becomes inoperable. And the accompanying interpretive guidance related to this says that laboratory information systems or LIS procedures must be available to operators. Instructions should identify the individuals either by name or position to notify if the LIS goes down, or if a system error occurs. So that's regulation one. There's three total.

The second is the test report standard. So this is 1291. The laboratory must have an adequate manual or electronic system in place to ensure test results and other information are reliable, reliably sent from the lab to the destination, the final destination, be it a patient or doctor or whoever. The accompanying interpretive guidance for this is that if a laboratory uses an LIS, what security measures have been instituted to ensure that transmitted reports go directly from the device, sending the reports to the authorized person or representative? And who is responsible for using the test results on the requisition?

And then the third, this is the last. This is 1254A1. And this refers to the maintenance and function tests on equipment and instruments. So labs are required to maintain their equipment and instruments according to the specificity and to the steps directed by the manufacturer. So the interpretive guidance related to this say that each piece of equipment or instrument the lab uses, including those that are peripherally involved in patient testing, like in LIS, they have to perform and document maintenance as specified. And it includes everything from monitors, printers, modems. All devices must be maintained to ensure accurate, clear and interference-free transmission. The interpretive guidance offers specific probes to this for surveyors to help assess this. Are the components maintained according to manufacturer's instructions? When downtime is required to perform maintenance on LIS equipment, how are LIS users notified? So this is probably the very baseline expectation in terms of cybersecurity. But it is very minimal, which is one of the reasons we wanted to bring this to the group to solicit ideas and thoughts if there needs to be more vigorous or rigorous regulations or guidance related to this.

So a recent edition of the Dark Report had these recommendations from NCC, which is a group called National Computing Centre. It looks like they're out of England by the way centre is spelled. To be clear, these are not CMS regulations. These are just recommendations from experts in the field. And these are, again, fairly basic. And the reason this slide was included specifically for the conversation that follows, one of the things that we would ask is to give some thought and consideration if these type of safeguards should be included in the regulations.

So the recommendations include things like employing multi-factor authentication on external facing internet connections, segregate legacy operating systems from the network, backup files with multiple offline locations, create patches to address vulnerabilities, frequently trained staff and awareness of security threats, and then draft and rehearse incident management plans. So the questions we have for CLIAC on this topic is, would CLIAC recommend stronger regulatory requirements related to the cybersecurity protocols for the laboratory setting. What is the real world risk of maintaining the status quo, weighing the likelihood of a cyber attack on a given laboratory, and assessing the current existing incentives to prevent an attack? And underlying all of this, this is the balance we are always playing. Anytime we are making considerations of regulatory change, the sheer scale or size difference in labs that are subject to CLIA regulations is enormous. We have billion dollar mega corporate labs performing billions of tests, and we also have labs that consist of a single person performing one test. So we need to always thread that needle to make sure that our regulations don't overburden the very small individual lab community, and is a nice balance for what the real risk is. So along those lines,

we're also asking the cost of regulations that require the steps on that previous slide, what are the benefits of such regulations. How much time a laboratory would need to make these kind of changes? And then any alternate recommendations CLIAC may have, something like a study group, an RFI, anything like that. So that is the overview of that. And then I'll turn it back over to you, Jordan, for discussion. And Heather, do you want me to keep this page up?

CLIAC DFO: No, I'll pull it back up at the end of the session.

MR. GREGG BRANDUSH: OK, great. Thanks

Cybersecurity Considerations for Clinical Laboratories
David McClintock, MD

CLIAC CHAIR: Excellent. Thank you. I believe we have a presentation now by Dr. David McClintock.

DR. DAVID MCCLINTOCK: You guys all see my screen?

CLIAC CHAIR: Not quite yet. There we go.

DR. DAVID MCCLINTOCK: We're good? All right. So thank you all for inviting me to speak on this. Yeah, so I'm going to go through the cybersecurity considerations for the clinical labs today. Main thing for disclosures wise, I don't think I have really any manufacturers or products seen here, but if there are, it's just for presentation purposes only. No disclosures on my part. Main thing is that this is a huge topic, so I'm going to go through big things here. No way I can do it in 20 minutes, but I'll try.

So first thing just to understand for people is that cybersecurity is more prominent than ever. It's hitting a ton of different hospitals all over the place. It's becoming more and more common. And in fact, as we've seen here, hold on. What's going on here? Here we go. Hackers even hitting children's hospitals. This was something that we saw just last year. We had Lurie Children's Hospital in Chicago get hit. And I love this quote. There's a special place in hell for a person who attacks a Children's Hospital and disrupts medical care for thousands of innocent children.

This is the state that we're in right now. No one should assume that, just because you're a small lab, or you're out of the way or whatever, that you're out of it, that you're not going to get affected. This can affect anybody. Don't make assumptions on who can be affected. One of the things I want to talk about, and the way that I want to frame this talk today, is to go over this idea of what are the types of security threats that are out there right now, and how can you react to them, what are the things you have to consider.

I'm not going to go through all of these. Again, we only have 20 minutes, but I do want to hit six of them right now, going through these kind of major different threats that are out there and how they may affect the clinical laboratories. The first one to talk about is social engineering. This is a big one that we've seen a lot of today. Most of you should all be familiar with this idea of phishing, spear phishing, whaling, phishing, smishing, whatever you want to call it. The whole premise here is that it's easier to trick a human than exploit a technical vulnerability in a system. We ourselves are the weakest link here.

The idea here is that you're going to prey on human nature, emotional responses to go ahead and get someone to click on a link, or to respond to an email, or do something that will allow some human interaction to allow that hacker to get some sort of credentials in, or to get some sort of information from you so that they can begin to inject ransomware or get some sort of data from you. This is real. A lot of us see this. We get trained on this within our institutions. This is an example of one that came from-- the email did not come from Dr. Liron Pantanowitz at UPMC, but instead it came to a lot of us on a specific list.

This is spear phishing in action where a hacker was posing as him to say, hey, are you still active on these email accounts, I need your help with something. They hit about 60, 70 of us going to give talks at a conference. A lot of us knew Dr. Pantanowitz. And so actually, one person, as he was checking for his-- he was getting gas, checking his email quick while he was getting gas and clicked on-- he went ahead and said, hey, I am fine. What do you need from me? Got the email back saying, hey, I need you to give me a steamer visa gift card for a friend's daughter who's down with cancer of the liver. It's her birthday. She had COVID, all this sort of stuff happening, the travel for a friend's burial. It sounds awful. At this point, he was like, wait a second, this isn't him. And then we went through the effort of finding out and basically making sure everybody knew that this was a spear phishing attempt. But this is how insidious these can get. People try to really prey on your emotions.

We need training in this, so clinical labs are no exception for this. This is something where people need to be trained and understand all the intricacies of what this looks like and how you go ahead and begin to start detecting these really kind of

elaborate email schemes that come out. And not only just on email, but voice calls, as well, texting, all that sort of stuff. The next thing to discuss is this idea of third party exposure. The idea here is that we all use systems within our laboratories where our partners who run those systems have privileged access, not only to their system, but potentially, others within our networks.

The goal here for the hackers really is to target that third party, the less protected system in place, and then that will give them access to the primary target. For the clinical labs, we really got to think about things like middleware. We use a lot of different applications. And so the more applications you have within your laboratories, especially to support some of these homegrown systems, maybe some of these ones that are based on open source software, where you can have large groups helping to develop the software online, and then you use it for your own purposes, but maybe don't do the full security check on these. There's ways for people to sometimes build in back door things for these kind of software.

So you have to be aware of what software you're using and whether or not it's something that has a security risk involved in it. A lot of times, we may be using legacy instruments, legacy applications within your laboratory. You just don't want to upgrade this one instrument because it's been working so well for you. But it uses Windows XP, or it only has Windows 7 drivers, that kind of thing. There needs to be a way for you to understand that the risk of your system may outweigh the use of that system, and that you have to go ahead and potentially have a plan to go ahead and upgrade those systems to the most modern architecture that is out there.

So this is something that people need to consider as you think about all the different things in your labs, not just from your applications, but also your equipment, as well. The next thing to talk about is this idea of cyber hygiene. A lot of practices. So basically, cyber hygiene is this idea that users can actually take measures to maintain the system health and improve cybersecurity within their institutions. It relies on both the institution that you're in, as well as its users to work together to improve and maintain the overall cybersecurity posture or the organization.

The idea of what cybersecurity posture is really the security status of an organization's networks, its information and its systems. So when you look at cybersecurity posture, really, it's understanding that it's not just a matter of having good firewalls, but it's actually understanding that there's multiple things involved. You have the information security resources that you have, again, your people, all your hardware, the software, and more importantly, the policies that you have in place to help protect things, as well as the capabilities in place to manage your defenses and to react as the situation changes.

As was mentioned, for the clinical labs, we may have really small laboratories and then have large laboratories that are either big reference labs or part of a larger institution. All of them have their own cybersecurity posture that they have to consider. These are the five main tenets that everybody should consider, this idea of are you providing the proper user cybersecurity education so they don't click on links, so that they don't fall for these phishing attempts, that kind of idea, understanding that you shouldn't be sharing your passwords, writing them down, that kind of stuff.

Do you have the proper password policies and multifactor authentication in place so that people have to authenticate whenever you log into the system, versus having one login to do everything, in which point then, as we'll talk a little bit, gives people access to all your systems. Are you performing the proper third party risk assessments for cybersecurity? Are you doing that on a regular basis, or only when you think about it? The idea here is that this should be something that is a knee jerk reaction for everybody now performing these cybersecurity risk assessments. It should be known as a standard practice, not just something that you have to do because someone tells you to.

You need to be owning that as part of your main processes. The other thing that you have to look at is, are you following zero trust, and are you doing network segmentation. I'll talk about that in a little bit. And then are you are you performing routine secure and offsite backups, with the idea being that you can bring your data back? If you are compromised and all your current on site systems are compromised, can you actually bring your data back in an effective way, versus having to go ahead and only rely on those systems that were infected?

We also use, and we have to understand that there's this idea of cybersecurity controls. So as we build out our cybersecurity posture, we have to make sure that we have the proper cybersecurity controls in place. There's proactive and reactive cyber controls. The main idea being that from a proactive perspective, we're actually trying to stop these systems or stop the things before they go into practice. So the idea being that we're trying to hunt threats before they hit us. We're trying to train our staff ahead of time before we have an event occur.

We're performing ethical hacking, or what used to be called penetration testing, to go ahead and ensure that our systems are secure. We're constantly testing them going forward. It's almost like performing QC on your systems in a sense. And then we're proactively monitoring our network and doing endpoint monitoring of our devices to make sure that we're actually keeping track of what's going on, versus just waiting for things to happen. From the reactive perspective, Once something may get into our system, how are we dealing with that? That's the idea behind that. Do we have the proper

firewalls in place to ensure that maybe things get through one layer, but then don't get through multiple layers? Do we have the proper, say, spam filters or other things in place to stop us, so that way we have risky emails go to a different spot than going to users inboxes where they can see them? The proper password protections. There's other things you can put in, ad blockers or other controls to make sure that people don't go into the wrong websites.

Everybody needs to have antivirus and anti-malware software included, lots of different ways that we can go ahead and react to things once they come in. From a user of cyber hygiene practice perspective, what can we do? Labs should be looking at using core image machines or corporate standard builds. Even with a small laboratory, you might want to work with the IT group to ensure that you have a standard build that will allow you to limit what people can do on it from your staff. You want to make sure that you don't have the ability for anybody to install whatever they want on these devices. We've seen lots of different threats come through. Sometimes people just want to try something out. They're kind of wondering, what is this cyber currency stuff, what is cryptocurrency, not realizing that those applications sometimes come with malware already on them. And before you know it, you've introduced something, just because someone to try it out, not realizing that you wanted to block that and ensure that they don't do those kind of things. Making sure that you have all the, obviously, antivirus software, regular software updates going on, making sure that your people are either changing their password, or using proper password requirements. For example, a 15 character password, that's hard to break or hard to brute force. Using two factor authentication, that was mentioned as something that everybody should be doing nowadays, as well as remote monitoring PC use, network connections, and really determining who has access to your VPN, and on which devices. With those virtual private networks, we don't want to have every vendor under the sun using them, and we want to restrict who can potentially use them, and for what purposes.

From the perspective of mobile devices, if you're allowing mobile devices to hit your networks, really, you need to have mobile device management and have that software in place so that you don't have exchange of data and have the ability for those networks to mingle when you go ahead and use those mobile devices on your applications. From the organizational perspective, this is for most laboratories, as well. You should really be looking at how do you control your network access. So there probably should be things in place to make sure that you have at least a way of determining what devices can access your network. That's what's called NAC, or network access control. Do you have the ability to segment your network? So do you have a clinical network, versus a research network, versus a guest network for large systems? Or do you have the ability to basically have a public versus clinical network, so that way, if somebody gets into one network, they don't have access to everything? That's the idea behind that. And then the idea of monitoring the network traffic and control who's actually has access is a big idea. From devices and storage perspective, really, one of the big problems that we see with a lot of laboratories is that they don't have a full inventory and they don't track all network devices that they have, or all the storage media that they have. This is a big issue. Same thing with applications, knowing all your applications and who has access to them. It's a big effort to do this, but it's something that places really should be looking at doing. You want to make sure that you have encryption and password protection on all your devices and storage. Only provide those really strong permission based access and establish retention policies for your data, acceptable content policies so that people know what they can download, what they can't, what data should be retained at any given point in time, how long you retain your data, those sorts of things. And then from an application perspective, really, we're looking at requiring things like single sign on and active directory integration, disabling local accounts whenever possible, so that way, people don't have access to systems without having true accountability. No more machine accounts, ideally, if possible. Performing regular risk assessments on all your applications. The third party risk assessment shouldn't be done just once. It should be done regularly so that you understand what's going on and how that system is evolving. If it hasn't evolved appropriately, then integrating those security reviews as part of every supply chain and procurement process, so that you don't do it only when you think of it, but you do it automatically for everything that you bring into your practice.

From a cloud vulnerability perspective, we're using more and more cloud applications within the laboratory, and we have to understand that these vulnerabilities do occur. They've reportedly increased 150% over the past five years. And especially with digital pathology and AI systems, we're seeing these really get used a lot more today. Ways that you can go ahead and look at minimizing cloud vulnerabilities is moving to a zero trust cybersecurity strategy. We'll talk about that in a second. And then becoming making sure that your cloud vendor and other applications that you're using become certified by high trust or other cybersecurity certification organizations, with the idea being that you basically want a way of understanding whether or not these organizations have gone through a really comprehensive cybersecurity risk management review. The idea here is that, think of it as a CLIA or CAP inspection for these companies. They're going through and providing you certification, showing you that they are cyber secure, and you want to be able to feel, to trust that.

In terms of cybersecurity strategies, this is probably more common for smaller organizations right now. But a lot of places will still use this idea of a castle and moat strategy, where you focus on the strong network security perimeter for all of your data. The idea is that you're trying to keep everybody out, but unfortunately, once they get in, you have keys to the kingdom. So where you may have strong security on the outside, you really need to think about how do you do something if you have an internal actor. Or when somebody gets in, what do you do when they get easy access? So the main point

here is that, while this is something that may be effective for smaller organizations to begin with, the idea is that you really want to move towards a zero trust strategy where you really think about the fact that no one can be trusted. And this is not saying you don't want to trust your employees, but the idea being that, if they do get compromised and somebody does compromise their account, you're stopping people, either internal or external, from getting in. So the idea is that there's no central or single security perimeter moat, and there's no keys to the United Kingdom. And you presume the risks are present both inside and outside your organization. So overall, you're trying to stop all incoming connections and source controls and make sure that everything's verified throughout all layers of your network. The user devices have to authenticate themselves when you access, basically, every application within the organization. This is where single sign on makes it easier, but the whole goal here is that you don't want to trust anybody, from the CEO on down to your typical user.

Moving on. Another thing to consider for us is poor data management. Main concept here is that data management today is more than just keeping your data organized. You have to understand what is the right data that you're keeping, who has access to that data, how do you share that data, how easily accessible is it, and do you provide good tools to do that. All that needs to be taken into consideration. Just storing your data in a shared drive now and giving access may not be enough today. You have to understand what you need to do and understand how you're using that data effectively.
The goal here, really thinking about it, I stole this from Spider-Man, obviously. But the whole idea here being, with great data comes great responsibility. We're generating more and more data every day, so you have to keep that in mind. What you guys used to do may not work and having a hoarder mentality. Yes, this was my parents' garage at one point in time. It's not much better. But the idea here is that you have to be able to organize this in some way. Data management changes are really important when we start considering digital pathology. Glass slides have been traditionally very hard to hack. In general, you only had one or two patient identifiers, only one copy of the slide. And so the person viewing it would have to know his pathology to even know what's going on with the patient. Unfortunately, digital slides are more easily distributable. They have metadata wrappers that have a lot of information about the patient and have varying degrees of patient identifiers. And if you start annotating those slides, you can actually maybe know what's going on with the patient. So that's much more actionable DHI than having a glass slide by itself. So really, we have to make sure that we understand, as we move digitally for digital pathology, is making sure that people have the ability to stop improper access or use of clinical slide images. Make sure that there's actually the proper de-identification processes in place for sharing them, and for using them for education and research, and make sure that we don't have the slide labels going along with that from a clinical perspective.

Finally, let's talk about post-attack procedures. We have to think about what we need to do for downtimes now in the future. People have to really consider what happens in the event of a cyber attack, and how will this differ from your current lab downtime procedures. The main thing to consider is that lab medicine pathology practices require network connectivity now for almost everything that we do. A lot of places have moved over to voice over IP type phones. You don't have typical analog fax machines, phone lines anymore. We use teams or other types of applications to chat with each other. And so the problem is that, when you have a ransomware attack, one of the first post-attack responses is to shut down the entire network. When that happens, everything that you were doing digitally goes away. And so for pathology in general, we're all excited about going digital. But when that happens, you no longer can do your work. So you need to have a way to fall back to paper and glass. Harder for the for the clinical labs, the main lab medicine labs, because of the way that we're so reliant on these instruments. But I just say, for people going to pathology, don't throw out your microscopes yet. That's going to be your way of still doing your work when your lab goes down. Things we have to consider when these attacks do happen. You have to strengthen your lab preparations. So cyber attacks can debilitate hospitals and labs for days to weeks. And that's the main thing. Don't just think it's going to happen for a few days. Be aware that these can go down for multiple weeks. We've seen places like Lurie were down for weeks. Vermont was down for weeks. Others have been down for weeks. We've talked about this.

Labs need specific post-attack procedures that address how you react without any network connectivity for long periods of time. You also need to change your business continuity plans to make sure that you include which lab systems are required, which lab systems are required when, to help with bringing those systems back online. You don't want to bring back these kind of esoteric, smaller systems when you need to bring back your LIS first, all the middleware systems that support that LIS, integration systems, that kind of stuff. Have an idea of what all those systems are so you know where that's at. That's included for both the enterprise solutions, where you want to make sure your lab system is included in that first tier of systems that may come back, versus a small laboratory, you have to understand which systems that you need to bring back when that happens. And again, I can't say this enough. We need to make sure that people are doing the proper third party risk management reviews, what we call TPRM in the business, for all their systems. So if you have both internally developed and externally purchased solutions in your practice, you need to make sure that you're doing these third party risk management reviews so that what's going on, where are the gaps in your systems, how cyber secure are they, really. You want to do that kind of work, and you may have to do that through third party. Again, there are third party vendors that provide these services for you. And ideally, you want to subject all the systems you have to this kind of review.

Because you may find out you have these legacy systems that are really not cyber secure and a real risk. Some of them, you may decide that you just don't need anymore. And that allows you to really help streamline your applications and processes. So the main parting note here is that cyber attacks are real. They can decimate your laboratory. We've seen this over and over again. This was the Vermont cyber attack that was really well published on in 2021. I really encourage you to go through and see some of the articles that happened, understand how much it cost the institution, all the effects that occurred to them. And more importantly, there's actually a series of five publications that go through this in AJCP that really coordinate and talk about how they had to coordinate all the different efforts within the laboratories. There's a podcast on this. You can get more information. We have a review article, as well, out there about the clinical laboratoriesthat so you can look at and understand to know what things you need to think about and how you can react to these cybersecurity strategies. And in general, the main thing to understand from all this is that there's lots of cybersecurity risk today. There's no 100% secure system. And I have an old Mac classic behind me. You can't see it with the background. But that would be totally secure because they don't have any internet access. But that's also not usable in today's day and age. So you have to make sure that you have the right systems in place, using cybersecurity principles so that way you're constantly QMing all of your systems. So equate that to, basically, bringing into your lab is what you need to do today. In general, the recommendation here has become part of the process. If you have information security teams within your organization, become part of that. Know what they do. Understand the process for that. Because at some point, you will likely be part of a cyber attack, and it will suck. It will be terrible. It will break things down, and it's the most stressful thing that I've heard from people happening to a hospital system in general now. It's terrible. So make sure you are properly prepared, so at least it won't be as bad when you go forward. So with that, I will finish one minute over. Sorry about that.

CLIAC CHAIR: Thank you very much. Yeah, it was a great presentation. Particularly love the last gift you included in that. Got a lot of smiles in the panelists. I believe we do have at least one public comment. Right, [CLIAC DFO]?

CLIAC DFO: Yes, we have a public comment. Dr. Diana Cardona will be providing the public comment from the College of American Pathologists.

CLIAC CHAIR: Great. Hi. Good morning.

Public Comments

DR. DIANA CARDONA: Yes, my name is Diana Cardona. I'm a practicing pathologist at Duke Health, where I'm also a Vice Chair and Associate Medical Director of the Health System's Clinical Laboratory. I'm here representing the College of American Pathologists today, and I truly appreciate the opportunity to provide this statement to you, the CLIAC. As the world's largest organization of board certified pathologists, and the leading provider of laboratory accreditation and proficiency testing, the CAP serves patients, pathologists and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

The CAP strongly supports efforts to protect health data and the continuity of care from cybersecurity attacks, and understands the need for policy solutions. Cybersecurity attacks can and do affect every entity in the health care community. Hospitals, medical practices, laboratories, patients, and private and public payers all must exchange health data with each other to diagnose, treat and report diseases. This data is critical to patient care, and as such, a profitable target for bad actors. However, adding cybersecurity requirements to CLIA regulations is incorrect and insufficient approach. CLIA is intended to regulate the core functions of the clinical laboratory. Regulatory requirements beyond oversight of laboratory accreditation or certification and testing would be out of the scope. In fact, other government agencies, such as the FDA, Cybersecurity and Infrastructure Security Agency are already working to establish regulatory requirements. These current efforts would protect individuals, specify the defense measures that covered entities need to implement, and outline the responsibilities of covered entities in case of cybersecurity attacks. An effective policy to thwart cybersecurity attacks entails an all of government approach, working collectively with all of industry. These efforts must include funding to support the implementation of new security measures, and to ensure consistency across government agencies' requirements. Laboratory systems, which include laboratory information systems, are connected to and part of wider hospital systems. Data is and must continue to be exchanged between ordering physicians, laboratories, patients, and when appropriate, public health authorities, and payers. Each of these entities has a role to play in securing health data. Data is not siloed, and cybersecurity solutions shouldn't be either. Continuing to address cybersecurity in a piecemeal fashion, singling out individual industries or components will likely not increase security of our health data, but could result in conflicting regulation, unnecessary costs, and increased burden. Effective cybersecurity solutions will necessitate rules and standards that are uniformly applied across the continuum of health care data exchange. However, the CAP does request that CLIA, and CMS more widely, review and discuss with the laboratory community concerns related to cybersecurity attacks, and the gaps that could potentially be addressed with regulatory action. For example, one of the most significant risks is documenting that a lab has received orders once systems go down. Some redundancy should be encouraged, while not being too prescriptive. This could entail parallel or backup systems involving paper based orders or records. Any guidance should be system wide and constructive, rather than punitive. It should also be

included a time frame for integrating paper based records into electronic systems once they're back up. Federal funding should be included to help laboratories implement the technology needed for compliance, as cost is the largest barrier to laboratories updating their information technology systems. Thank you for the time to discuss the CAP's concerns and recommendations, and we welcome the opportunity for further dialogue.

CLIAC CHAIR: Thank you.

CLIAC DFO: And as a reminder for all CLIAC members and all audience members, all public comments are online at our CLIAC meeting page.

Committee Discussion

CLIAC CHAIR: Great. Thank you for the comments. [CLIAC DFO], do we have any others? I don't think so. Right? OK. So we could move into the committee discussion. And I'll start off by asking if there are any questions for David who just gave that great presentation, and then yeah, if you bring up those, the questions for CLIAC to discuss. Let's kick it off. How do people feel? How do people react? I have a couple of comments that I wanted to speak to, to set the tone. I just want to make sure, as we're discussing, we think of the full spectrum of laboratories from the small individual laboratories, all the way to the larger ones. I suspect the hospital based labs, the larger laboratories have, probably, a separate IT infrastructure that manages the majority of this type of efforts. And so, obviously, we're a part of it. We're aware of it, but it's not necessarily under our control. And I just want to make sure we don't forget about the smaller independent laboratories that may not have that infrastructure in place. So all right. I'll kick it off to the committee. Any questions, comments? OK, [CLIAC MEMBER].

CLIAC MEMBER: Good morning, everybody. I was a little surprised by the CAP's comment, and I think it was a good one. It just hadn't occurred to me because I guess my perspective is that we are not doing a great job with cybersecurity. There are many aspects of laboratory computing that put us at risk. In fact, some of the federal regulations themselves are challenging. And I'm referring to the fact that FDA regulated and certified devices are unable to be patched with security patches, at the risk of invalidating those platforms. And this has been a real challenge for many of us in the community. The other aspects of this are just, how do we deal with our data across networks. I have been really surprised that most laboratories send lab data in clear text through their networks. Now, I don't know if that really falls on CLIAC. Show. I was kind of titrating between David's presentation, the comments by the CAP, and then the regulations that we have in the CFR. Because there seems to be an intersection there that this group could potentially speak to. But I do think what we don't want to do is create confusion. And I think we do need to advocate for best practices, and perhaps even some level of inspection at the level of CLIA to validate and certify that labs are at least operating at a certain level. So I think this is really important. I think CLIAC does have a role, and I'm interested to hear what other's thoughts are on what that role should be so that we're not stepping all over each other.

CLIAC CHAIR: Thank you. [CLIAC MEMBER]?

CLIAC MEMBER: Thanks. I was slow to get my hand up, so now I have to follow [CLIAC MEMBER] on this. But [CLIAC CHAIR], it was really a comment back to your opening statement. And yes, the smaller labs are one. And I wholeheartedly agree with your comment about what's in the laboratories' control. But what I also will discuss is within what the spirit of what you were talking about as governmental labs, as well. So there are lots of input that goes into whether they be cloud based systems, which is what we talked about, and/or cybersecurity. And that continues to evolve at the federal, state, and local level. But it is varied and really depends on what jurisdiction you're in. There are jurisdictions that will allow a lot more than others, and so I think that's something for the committee to consider because it might be difficult to recommend an entire standard that certain laboratories and governmental jurisdictions may not be able to abide by. Thanks.

CLIAC CHAIR: Thank you. [CLIAC MEMBER]?

CLIAC MEMBER: So yesterday, we had a discussion about whether data was considered a specimen. So if data is considered a specimen, then I think we have to think about the custody of that data, in which case CLIA, I think, would have a responsibility to make some statements about cybersecurity. And as for small practices, I realize they do not have IT departments, but you don't necessarily have to maintain a full time IT department to have a consultant come in and make sure that you are secure. You can also introduce a concept of-- I don't want to use the word waive, because it has so many meanings for CLIA. But you can use the concept of making small labs exempt based on the number of specimens that they process. So I think it is something to address. The world is only becoming more and more complicated. And if we sit back and say, well, we're just going to ignore that because it's too complicated to deal with, the world is going to pass us by. And then the FDA might come in and take over, which has not been received well within the pathology community.

CLIAC CHAIR: Thank you. [CLIAC MEMBER]?

CLIAC MEMBER: Yeah, I wonder if there's a really practical tool that, particularly for smaller labs, that this group or a related group could come up with, so that something that we could send out to all labs is kind of a just a one pager. Here's the risks. Here are possible mitigation solutions. Probably don't want to get into recommending different companies or that sort of thing, but just a practical, informational sheet that we could send out that would be helpful for, again, particularly, the small laboratories.

CLIAC CHAIR: Thank you. Yeah, I could share some of my comments. I really struggled with this. And I actually very much appreciate CAP's comments because, obviously, hearing, knowing the cybersecurity risk in general, hearing the presentation, of course, there have been some pretty significant, high profile health industry breaches in the past few years. I would say ignoring it doesn't feel right. At the same time, I don't feel like, as a past and current lab director, I have the skill set to be able to navigate this. And in fact, I think I've been blessed by being in large organizations. We always had a much larger true expertise outside of the laboratory system that we were beneficiaries of that expertise. I didn't have to worry about it because someone else with the true skill set did. So in one way, I don't think doing nothing feels right. But I'm also cautious about how much we can realistically put on laboratories to own this, given the skill sets, current personnel that are employed by laboratories to avoid it being overly burdensome. As we move forward, I'm trying to just kind of frame what flavors of recommendations. We can make. So first, certainly, we can make a regulatory or a regulation recommendation of being slightly more specific in terms of what laboratories should or shouldn't do. I think education could be also a recommendation we make, in terms of making sure laboratories are fully educated on the risks, and through those education modules, maybe make some suggestions and things like that, or point them to best practices. Or the third flavor is learning more. What could we do? Make a recommendation as a committee. Do we have a workgroup or an RFI that was suggested to learn more about what is the status of cybersecurity and clinical laboratories today, and then consume that information and make more stronger recommendations in the back end. So I see a couple of questions. Heather, if you can go back up to the questions we're supposed to talk through, we'll go [CLIAC MEMBER], [CLIAC MEMBER], and then we could start marching through some of these questions. I will comment. We have until 12:40 Eastern time to complete this. So at some point, I'll start to push us towards making actual recommendations. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: Sure. And [CLIAC CHAIR], I think you're kind of aligning towards some of what I was going to comment on. I did want to mention that some portion of the excellent presentation that we sat through mentioned that there's a good portion of cybersecurity attack that directs towards social engineering. Or I might not be getting the terminology right. So perhaps something that maybe, I guess, a practical element of recommendation as you were leaning towards could be towards recommending that there be a educational element for laboratorians towards the social engineering aspect of cybersecurity. And I think that that would be a very practical element that would be within the control of the laboratory. And then we've had a number of recommendations that were towards the CDC in providing that education. And I think that we saw in prior presentations that the CDC has some really great educational tools. And so I think that maybe either a two prong recommendation or two different recommendations might be able to go hand in hand in making some very practical recommendations that are within the laboratory's control.

CLIAC CHAIR: Great, thank you. [CLIAC MEMBER]?

CLIAC MEMBER: Yeah. Thanks, [CLIAC CHAIR]. I had two comments. And part of the first one was related to the current discussion of cybersecurity in CLIA. Because when I read some of this, it's not really about cybersecurity. It's about downtime procedure. Is there actually cybersecurity in CLIA? Is the wording there? Because what I'm hearing is really not so much about that. So that was the first comment I wanted to make. And with that in mind, maybe figuring out how do we put specifically discussion of cybersecurity in CLIA might be the way we start versus telling the lab, necessarily, what to do. So that was the first one. And then the second comment is related to the fact that a lot of people have mentioned. Is it the lab that's supposed to be doing all of this? I'm wondering what requirements are in the joint commission guidance, because I don't think the labs would do this independently of the rest of the hospital. So is there a way to align, to make recommendations where it's more about aligning what the hospitals are supposed to do under the joint commission with what the labs are supposed to do under CLIA, so it doesn't just necessarily fall on the lab? Yeah, we can't ignore it, but the lab doesn't function independently of the rest of the hospital. So there must be some alignment there. And maybe part of our recommendation is looking at those different pieces and putting them together.

CLIAC CHAIR: Yeah. Thank you for that. [CLIAC MEMBER]?

CLIAC MEMBER: Thank you. I look at this as an issue of continuity of operations. And I think that's a very important thing for everybody to take care of and be prepared for it. But it doesn't stand alone because there are other threats to your operations that will put you at risk of not being able to meet your mission, as well. So CLIA does not get into those other risks either. So I'm debating here whether it's really part of CLIA's role to get involved in this. But I really do feel it's an important issue, and I could see where more people need to be made aware of it and to have plans for it so I could go that direction. Thank you.

CLIAC CHAIR: Thank you. And [CLIAC MEMBER], before I call on you, just for the rest of the committee, please just review. The questions are on the screen right now, and see how they influence your comments or thought process. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: Yes, I'm actually the third in a trio of consecutive comments about the downtime side of this, because as I'm listening both to the initial presentation, the concerns raised by the CAP, and our own deliberations about what is CLIA about, I perceive basically two broad domains. The first is the hardness of cybersecurity and security in the first place, including the social engineering. And the second is the laboratory's responsibility for risk assessment and mitigation. And I think to echo what [CLIAC MEMBER] just said, the risk assessment and mitigation, we were discussing yesterday for a different reason. It falls within responsibilities of continuity of operations, and that might permit this committee to sail close to the wind in terms of what the lab's responsibilities are for safety and continuity, without getting into the institutional, small or large, about the actual mechanics of cybersecurity as an exercise itself, if there's a hand wave at smaller labs engaging third parties to advise, that's one way perhaps to address the smaller laboratories.

CLIAC CHAIR: Thank you. [CLIAC MEMBER].

CLIAC MEMBER: Finding you. There we go. I guess my question, first of all, [CLIAC CHAIR], is, are we allowed to suggest adjustments to the language in the Federal Register? Is that part of the purview of CLIAC? So if we look at those recommendations that [CLIAC DFO] has been putting up, some of these are pretty old in the teeth. That first one, you need to have procedures to get your LIS back on line. I'm not even sure what value that provides for anybody. It's really not helpful. And then if we look at the 1291 second part, it seems that it would be very easy to modify that by saying, not that we just ensure that it's transmitted, but to ensure that it's securely transmitted. It's a very subtle change, but it's a big change and maybe speaks a little bit to the points that [CLIAC MEMBER] made. So I guess I have a couple of-- my first point is a question. Are we allowed to provide some suggested edits to this language? If we are, I think there are some very simple things that we can adjust that will start to put cybersecurity into some focus without getting to the level of institutional policies, or procedures, or processes. Because it is an at risk situation for the laboratory. We are an actor who is highly at risk, and we provide vectors for entry that are probably larger than any other part of the organization, unless you want to get to the internet of things, and hacking IV pumps and stuff like that. We have hundreds of devices, so I do think that we have to take some ownership to this. And again, also to [CLIAC MEMBER] point, it made me think of not only the Joint Commission, [CLIAC MEMBER], but also, what the CAP says about this, which is pretty extensive. So on the one hand, they said don't regulate this, but on the other hand, they're making a lot of recommendations on how this should be regulated. And I'm not sure we have enough information about that. So maybe a working group or a study of the state of laboratory security in modern times is an important thing for us to look at.

CLIAC CHAIR: Yeah, I think very good points. And to try and keep us of out of the weeds, not that being in the weeds is bad, but I think to up-level your recommendation, [CLIAC MEMBER], would be that CLIAC could recommend that the existing regulations that fall under the cybersecurity umbrella be updated for our current environment. We don't necessarily have to do that here. We could provide some guidance, of course. But I think that's a really good call out and recommendation. If I may be so somewhat controversial, I'd also like to put forward a recommendation and see how everyone reacts. These are the rigs that are falling under the cybersecurity bucket. I think we're all reacting to them that they're not capturing the broader essence of cybersecurity. They're really transmission, downtime, recovery, things like that. And to plant a flag, and what I think would be a really good next step in terms of further hardening clinical laboratories from cybersecurity threats, is maybe to recommend a regulation that requires laboratories to have a cybersecurity plan. The details of that plan, I think, I would caution to be overly prescriptive, and it can be deferred. So for the laboratories that exist in hospitals, they would just need some kind of document from their IT systems of what the cybersecurity plan is already. They don't have to adopt. They don't have to create one themselves. But also, by having that reg, it will require smaller laboratories to develop a cybersecurity plan. And how they do it is entirely up to them so that it could fit into their finances and their operations. But I think net net, having that reg would raise the tide a bit. Reactions?

CLIAC MEMBER: Is, I guess, going back to my question, cybersecurity defined somewhere? What do we mean by that?

CLIAC CHAIR: So good point. I had it written down and I didn't say it. But I think that definitely needs to be supplemented with some kind of education to answer exactly your question. What does that mean? What does a good cybersecurity plan contain? What is it? What are some best practices? Wrapping it around within education I think would be really important. And I think it gives the flexibility of not being overly burdensome. You have to have a plan. And years from now, as we ratchet this up, maybe it could become a little bit more prescriptive. But right now, there's no requirement for that plan. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: Yeah, I was just going to add to that, [CLIAC DFO], that I think that's a really good idea. Having a plan is always a good thing. We are supposed to have plans for disasters, not only in our hospitals, but also, in our homes. I

know our health care system extends natural weather related disasters, not only in the hospital to our homes. Because if we're screwed up in our homes, we can't go to work. So there is actually a continuity to this. So I think having a plan is a really important part of this. And you're right. We don't have to make it up. We can state that we have an adopted plan. It comes to us from above. I'm really honored, I guess, or proud to be from an organization that takes this really seriously. And we not only plan. We drill. So last year, we did a five-day-long simulated cyber attack, where this happened on day one, that happened on day two, that happened on day three. And every time you caught up with yourself, someone pulled another rug out from under yourself. And we learned so much about our weaknesses. And we work really hard at this, and we had a lot of weaknesses. So drilling is also part of a plan. We do this for fire prevention, for God's sake. And the modern fire is cybersecurity attacks in data loss and interruption of patient care. So I really like your idea and how it connects to education. And I agree. I think it also does come back to the regulations and making sure that they address this in a modern sense, because that's not modern language that we're seeing on the screen. I've been teaching that for 25 years.

CLIAC CHAIR: Perfect Thank you. Yeah, and [CLIAC DFO], I see you, obviously, typing away. Just to call out that second recommendation to marked comments earlier, that we recommend that the existing regs be updated with modern in the context of modern cyber-ness, for a lack of a better term. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: So I think we might-- even though you don't want to be particularly prescriptive, one thing is to look at what NIST, the National Institute of Standards and-- I forget what the T is. Technology, I think-- what NIST has, because they certainly do have recommendations on levels of encryption and so on that HIPAA actually refers to. So we might see what is there that we could fall back on, because I like the idea of saying you have to have a recovery plan. But I think we need to give it some strength, a recovery plan that addresses transmission of data during downtime, minimization of downtime and recovery. I'm not saying that everybody has to go out and buy ransomware insurance, but it's probably not a bad idea.

CLIAC CHAIR: Yep. Thank you. [CLIAC MEMBER]? You're muted.

CLIAC MEMBER: Sorry. I think we need to make sure that we're emphasizing the value of the cybersecurity knowledge and all of that, but not that we're duplicating or doing something outside what the organization already has in place. So I would like to make sure that we're including that. And for instance, I remember when I was at Lifespan, we were talking about physicians entering their own results. Some were concerned about accuracy of them entering results, but we weren't concerned about, potentially, them getting hacked. So I think there's a lot of overarching things that laboratories might end up being responsible for in that sense, where we just couldn't manage that. And I don't want to have that undue burden put on labs. But I do think that there are-- like our IT team at Lifespan, we were constantly getting quizzed. They would constantly be sending out fake things to see if we'd click on them, and all this other stuff. So there were those resources already in place. And I know they would be upset if we tried to do something on our own. And even when we would purchase a new piece of equipment, the IT component that Roche, for instance, had to go through was ridiculous for us to bring in an instrument. So I think that I don't want to be duplicating or overarching where it's not necessary. And how can we help, potentially, labs that don't have those resources to make sure that they're doing the right thing, or know where they can go? That would be what I would be more concerned about.

CLIAC CHAIR: Absolutely. And I think, [CLIAC DFO], as you're writing down the information for agencies to consider, I think cross walking and making sure that we're not being duplicative with other regulations from other agencies that impact health care organizations, be them hospitals. So I don't know. Does JCO have these regs already in place? And I would say, if yes, you could almost use that as an exemption for having a cybersecurity plan in the laboratory if your hospital is under JCO or something like that. Because I think we're all being very sensitive. The labs may not have the expertise, probably don't have the existing resources, and we certainly don't want to be duplicative. Go ahead, [CLIAC MEMBER]. I see your hand up, as well.

CLIAC MEMBER: Yeah, I think we're all on the same page, or moving in the same direction. The thing that I would like to point out is, I can't tell you when the CLIA regulations that are down below, when they were written. But I just in my career as a laboratorian, at one point, all of the statement of an LIS was truly a laboratory information team, or system, or whatever you want to say. We took care of it in the laboratory. As the years go by, written in 1988, as the years go by, that's not the case. Every place that I'm now a part of, the, quote, LIS team resides in information security. So that's something that I don't know if the first recommendation, CLIAC recommends a regulation that requires laboratories to have a cybersecurity plan. I don't know if that should even have laboratories in there, just because, is there a cybersecurity plan in place? That's one of the notes that I took down was, I don't even know all the avenues that our current information system has right now. I think [CLIAC MEMBER] brought up several that are in place, where I work, phishing and all that stuff. But to be honest, I don't know. I know we have an extensive-- when we bring on instrumentation, we have an extensive process in place that screens those. But to be honest, I don't know what they're screening for, particularly. I think for the laboratory, one of the areas that I see is, the most extensive cybersecurity threat that I hear about from other laboratorians is vendors, or a thumb drive, or something coming in, and they plug it in

instruments, et cetera. And that's where usually bad things happen. And then I would just like to say that we're talking about instruments and things like this. But one of the things that I think laboratories are good at for a short period of time-- I'm not going to say weeks and weeks and weeks-- is, the lab, unfortunately, is pretty good at short periods of downtime, because we're down a lot in the laboratories. It could be for general maintenance, et cetera. So I do think that the laboratory has an understanding of the risk and how to handle it. But two weeks at a time, now, that's a totally different topic. So I think, really, to wrap things up, I think this is much bigger than the laboratory. And I don't know if there's a communication avenue with IS and lab that can be written in to these regulations. But I don't know. That's my two cents.

CLIAC CHAIR: Yeah, I think that's a great point. And at least my kind of vision of what that proposed requirement of having a cybersecurity plan would absolutely include those relationships and different organizational structures. So for example, in places I've been in the past, or even now, I would expect that. I would ask, say, IS to say, hey, can you give me a one, two page summary of our cybersecurity plan. What are you doing to prevent attacks? What are you doing to recover? And to be honest with you, that, to me, the way I envision this reg, that would satisfy it. I think the value there, for me as a current and past lab director, I'm super confident we have a robust cybersecurity plan. A way it would benefit me is that I have one or two page summary where I actually have a little bit more information as to how we're protected. Just give me more insight into how we're protected. It also will raise the tide for labs that don't have a cybersecurity plan and force them to generate one. And again, without being specific, I still feel very comfortable bringing a lab that has no cybersecurity plan to a weak cybersecurity security plan, because net net, we're hardening the system. It's not perfect, but it's hardening the system. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: Well, as you guys can tell, I'm very passionate about this. Probably, one of the reasons I should have been hired to work here with you all, because this does keep me up at night. And if it doesn't worry you at all, you should think about it harder. And to [CLIAC MEMBER] point, I think it's a very important one, [CLIAC MEMBER], but I think it actually increases our risk when this stuff gets pushed up into IT. They don't understand these instruments. They don't understand the communication pathways, and it actually increases our risk. It doesn't necessarily decrease it. I think the place that it helps us is that we're more tightly aligned with the security groups. But to other points, it's also what makes it harder to get our work done, to bring in a new instrument. The amount of effort that goes in to push stuff through these information, privacy and security groups is absolutely brutal. I don't think that's part of our discussion here. But aligning closer to IT is both helpful and hurtful in my experience.

CLIAC CHAIR: Great. Any other questions, comments, recommendations? OK. So we do have a couple of draft recommendations up on the board. One of them is recommending a regulation for just having a documented cybersecurity plan with the education to surround it. I don't know, [CLIAC DFO], if it's helpful. And correct me if I'm allocating this incorrectly. But recommend that CMS create the regulation and CDC create the education? But I think that would be one recommendation. I think it's important that they go together. And then the second recommendation is recommending, I guess, to CMS to review and update the existing regulations to reflect modern society. Obviously, the internet wasn't even invented in 1988. Or maybe it was invented, but not widely used. So clearly, there's some catch up there in terms of the verbiage and spirit. And then the last one is CLIAC recommends a workgroup to assess the state of cybersecurity. And we can talk about that at feels. I don't know. We'd have to talk about it and see how much, what other information we would want beyond the first two recommendations. With that, let's start with the first recommendation. We have one up there. Is there any quick modifications, anything you want to do before ask for a motion? I know it's hard.

CLIAC MEMBER: Yes. I just want to say, if you Google NIST and cybersecurity, it comes up with a nice list of things to address, and they're pretty generic. Risk management, identity and access control, data security, which is protecting confidentiality, integrity, and availability. Security awareness training, which we've all been talking about. Maintenance, data backups. Technology management, incident response. Have a security architecture and response plan in place to detect and respond to incidents. Incident recovery, and non-repudiation. Ensure that the sender of information has proof of delivery, and the recipient has proof of the sender's identity. I think it would be good to mention some of these things.

CLIAC CHAIR: Yeah, I think it's well said. Again, we like putting that degree of specificity into where Heather's putting the information for agencies to consider, to give the agencies the greatest amount of flexibility of addressing it within--

CLIAC MEMBER: Right. Right, you addressed this, but these items you specifically have to address.

CLIAC CHAIR: Yeah, I think that's great.

CLIAC MEMBER: You have to have an SOP for them.

CLIAC CHAIR: Any other questions or comments before asking for a motion on the first one? All right. Do we have a motion?

CLIAC MEMBER: I move.

CLIAC CHAIR: Thank you. How about a second?

CLIAC MEMBER: I'll second.

CLIAC CHAIR: All right. All those in favor of approving the first recommendation, please raise your virtual hand. Looks like we have a solid majority. Thank you very much. So that passes. OK, if you can now lower your hand, because I'm going to ask you about the second one. The second recommendation, CLIAC recommends the existing regs related to cybersecurity be updated to reflect modern laboratory security issues. Any edits before asking for a motion? [CLIAC MEMBER].

CLIAC MEMBER: Yes, I'm assuming this recommendation is intentionally silent on how that review is going to be done. And I would recommend keeping it that way. I just wanted it to be an overt decision by this group that we're not asking for a workgroup or something else. Just say that it needs to be done, and then leave it at that, which is my recommendation.

CLIAC CHAIR: Exactly. Any other comments?

CLIAC DFO: So I changed the wording, and may need help from [CMS EX OFFICIO] on this one. Because we don't call out cybersecurity as you've seen and [CMS EX OFFICIO] presented in the CLIA regulations. So is this that may be related to cybersecurity appropriate, or is there a different way? I think we get the gist of what the conversation is, but there are no regulations right now directly related to cybersecurity. It's just these here that we had talked about. So I'm happy to make any edits, or if that's good.

CMS EX OFFICIO: No, I think that's fine. The recommendation that I'm hearing is the existing regulation needs to be updated to explicitly include cybersecurity elements.

CLIAC MEMBER: But I think if you called it information management, that that would be broad and include cybersecurity.

CLIAC MEMBER: And put cybersecurity in parentheses or something because it's not even in there. I think we need to mention it because it's not in there.

CLIAC MEMBER: Information management, open parentheses, e.g. Cybersecurity.

CLIAC MEMBER: I don't know if anybody has insight into what the term of the future is going to be. We could use that.

CLIAC CHAIR: OK. How's everyone feel about this? CLIAC recommends that the existing CLIA regulations be updated to reflect modern cybersecurity and information management issues. See one virtual thumbs up. Is there a motion?

CLIAC MEMBER: So moved.

CLIAC CHAIR: Is there a second?

CLIAC MEMBER: Second OK. You know the drill. Raise your virtual hand if you all in favor. And again, saw the majority. Thank you. It passes. So with these first two, how do we all feel about the need for a workgroup? I know we were talking about it. We threw it up there. My personal gut feeling is probably not necessary at this point, but leverage the greater intelligence of this group. Comments?

CLIAC MEMBER: I don't think it's necessary.

CLIAC CHAIR: OK, have that comment. I see a couple of heads shaking. All right. Well, hearing that, I would suggest let's remove that. Any other questions or comments on this topic?

CLIAC MEMBER: I guess I'd like to just suggest we revisit it in the face of the information discovery that we've alliterated below about information from other agencies. I don't know if there's a way that we can synthesize that as to the present state without going so far as to develop a working group. But I'm with you. I think the last thing we want to do is generate working groups that we really don't need because something's already been delineated.

CLIAC CHAIR: Great. I think it's a good call out. I'd love to revisit this someday just to see how things have maybe changed over the years in terms of regs, reaction to regs, implementation, et cetera. [CLIAC MEMBER], your hands up.

CLIAC MEMBER: Yes, very briefly. I think we've touched upon it, but I think it's worth making sure that the minutes of this discussion record our enthusiasm for educational materials being made available.

CLIAC CHAIR: Thank you. And [CMS EX OFFICIO].

CMS EX OFFICIO: Yeah, I have a question with respect to the comment about other organizations that have requirements that may be applicable to the lab, so there's a general CLIA requirement that says labs need to be in compliance with other federal, local, state regulations. Are there other entities that would find a lab in violation of some cybersecurity element, or some system security element? Because that's a direct tie-in to our requirements. But if it's just a recommended best practices, I'm hearing that we need to make sure that there's an alignment and not conflict. But it's a little different in terms of being able to enforce it.

CLIAC CHAIR: OK. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: Yeah, I know that the FDA, [CMS EX OFFICIO], has got significant comments on validation testing, system security, so forth and so on. So I think you're right. And that's kind of the point here, is that there's a lot out there that we probably don't have pulled together into a white paper, or a working manual that people know where this stuff is discoverable. It's very difficult to find sometimes. But as [CLIAC MEMBER] pointed out, you just go to the NIST, and there's a tremendously accessible list available to us.

CLIAC CHAIR: And that was also what I was hoping that educational materials that would be generated to help support this would do, or would help to identify, are there other agencies and regulations that are not directly responsible for labs that may cover labs, or may just be able to inform what are there best practices out there. And NIST certainly sounds like a great one, but there may be others. So I think that education piece would be really helping everyone understand what a plan is, what are the components, who, what regs are out there that may already cover you. Because, again, we really don't want to be duplicative here. [FDA EX OFFICIO]?

FDA EX OFFICIO: Hi. I heard that comment. I think FDA has been raised twice with respect to our requirements. We do have cybersecurity requirements, but I want to make clear, they have devices that a lab might be using or might be in a hospital being used. And those requirements relate to the manufacturers of those devices. We don't have anything that addresses what's been discussed today. So I just want to make sure that's clear. Although, certainly, if you use devices that are cyber secure, that might help with your plan.

CLIAC CHAIR: For sure. All right. We're 15 minutes ahead of schedule, I think, probably, the first time ever time I've been on CLIAC. Any other questions or comments, or should we just relish in this moment?

CLIAC DFO: I was going to suggest we could probably take a 15 minute break and come back at 12:40, because we do have a speaker that is scheduled. So instead of moving on, I suggest we just take a short break and come back at 12:40.

CLIAC CHAIR: Sounds like a great idea. All right. At 12:40 Eastern, we'll see you back here. And thank you very much. Really great conversation and a successful session. Thank you.

Proficiency Testing: Determination of Clinically Relevant Range of Value

CLIAC CHAIR: [CLIAC DFO], let me know when you think we're ready to go.

CLIAC DFO: We'll give it one more minute.

CLIAC CHAIR: Sounds good.

CLIAC DFO: OK, we can go ahead and get started.

Introduction to Topic
Angelique Daubert, MLS(ASCP)
Víctor R. De Jesús, PhD

CLIAC CHAIR: All righty. Our next topic today will be proficiency testing, determination of clinically relevant range of values. So we're going to start with an introduction by Ms. Angelique Daubert, a clinical laboratory scientist and branch manager in the Division of Clinical Laboratory Improvement and quality regulations and clearance branch at CMS. And Dr. Victor DE JESUS, the Acting Director of CDC's Division of Laboratory Systems. The introduction will be followed by a presentation on proficiency testing, measuring the clinically relevant range of values provided by Dr. Nikola Baumann, the Co-director of Central Clinical Laboratory and Central Processing at Mayo Clinic. After the presentations, we'll have some

time for some questions, committee discussions, as well as public comments. And I will turn it over to Angelique to kick us off.

MS. ANGELIQUE DAUBERT: Thank you so much. The regulations and clearance branch has the primary responsibility within CMS to look at proficiency testing program approval. Next slide, Heather.

This is just our normal disclaimer. If there's any errors made today, they are solely mine. Next slide.

So just to give you a kind of a broad overview of the PT program approval process, each year, the PT program has to seek approval or re approval for the program for the next calendar year. And the regulations state that they have to provide their application by July 1st of the current year. So CMS partners with the CDC to approve PT programs annually. And in general, CMS focuses on evaluating the information about program administration and proposed content for the upcoming calendar year, while CDC focuses on analyzing the data from the PT program's previous year's offering to assure that they have met the regulatory guidelines. Next slide.

What we're asking the committee to look at specifically today is the PT program requirements. So it's phrased a couple different ways in the regulations, but it's really looking at having the annual programs provide samples that really cover all the range of the patient samples. So for syphilis, serology, general immunology, the reg states that the annual program has to provide samples that cover the full range of reactivity, from highly reactive to non reactive. In routine chemistry and endocrinology, it states that the samples have to cover the clinically relevant range of values that would be expected in patient specimens. For toxicology, it's phrased just a little bit different. Samples are to cover the full range of values that could occur in patient specimens, and that cover the level of clinical significance for that particular drug. Next slide. In hematology, again, it covers the full range of values that would be expected in patient samples. And finally, in immunohematology it states that it has to cover the full range of interpretations that would be expected in patient samples. Next slide.

So this can sometimes be really challenging for PT programs. Where we see the largest challenge for them is providing those samples on the low end of the range. So there's some examples on the slide of analytes in the last couple of years that have proved to be challenging. And some of the reasons we get back from the PT programs of why it's a challenge is because samples have to cover multiple instruments, methodologies, reagents, and analytes. Sometimes a sample may cover 50 analytes. So at this time, I'm going to pass it over to Victor, who's going to talk a little bit more about the process of evaluating.

DR. VICTOR DE JESUS: Great. Thank you, Angie. And good day to all of you. As Angie mentioned, CDC assesses the performance of our US proficiency testing programs, which are approved by CMS under CLIA. We review PT program performance and provide a technical appraisal of program compliance with CLIA requirements, based on available PT data from the providers. And to do our analysis, we use reference ranges to inform this analysis. Next slide, please.
So Angie gave a wonderful introduction to reference ranges and what we are looking for in our analysis. So I'm going to share a few specifics of what we do. For each analyte, the values from the total population of the laboratories that participate in the PT programs, or the largest number of labs are recorded and compared to the reference range that we utilize. Next slide, please.

As part of our analysis, we expect that, of the 15 annual challenges that laboratories perform, at least one is within 10% of the lowest or the highest reference value to be considered in compliance with the regulation. Now, of course, CDC does not set these reference ranges. We utilize most reference ranges from the Mayo Clinic test menu website. And the link to that is on this slide. However, that is not inclusive of all the regulated analytes, and there are five analytes that are not found on the Mayo Clinic test menu website, which I will describe next. Next slide.

These are the five analytes which include blood gases, creatine kinase, MB isoenzyme, lactate dehydrogenase, isoenzymes, T3 uptake, and white blood cell differential. On this slide, you will find links to reference ranges that we have found that we utilize during our analysis. Next slide. Now, a little bit outside the box here is for white blood cell differentials. We don't have access to specific laboratory reference ranges. Different sets of challenges are sent out by the different providers based on the instrument that is used. And this is something that Angie alluded to in her presentation before mine. So the instrument used by the largest number of laboratories for most of the programs is what's essentially becomes a reference range for us. If one or two programs have a different instrument used by most of the laboratories, we still utilize the one used by most laboratories in the majority of the PT program providers. Next slide, please.

So, as you can see, our analysis would greatly benefit from additional information about reference ranges and how we can successfully utilize these reference ranges and source them, as well, to help us in our analysis for CMS's approval of proficiency testing programs. Angie, back to you.

MS. ANGELIQUE DAUBERT: Heather, I think there's one more slide. And the last slide is really about the questions that

we would like CLIAC to center their discussion around. The first question is, how should we determine the sample range for each analyte that a PT program should cover, taking into consideration the regulation terminology, clinically relevant range, full range of reactivity, level of clinical significance. And then in addition, the second question is, what are acceptable limitations to proficiency testing programs in meeting these ranges. So those are the two areas that we would appreciate discussion on. And at this time, I'm really looking forward to doctor Baumann's talk about clinically relevant ranges. Thanks.

Proficiency Testing: Measuring the Clinically Relevant Range of Values
Nikola A. Baumann, PhD

DR. NIKOLA BAUMANN: Wonderful. Thank you. And I am going to share my screen. Apologies.

CLIAC CHAIR: Just so you know, we see your email.

DR. NIKOLA BAUMANN: Yes, thank you. That's embarrassing. Very good. Well, thank you so much for the invitation to be here. And yeah, it's really my pleasure to discuss this topic, which was fascinating for me to really reflect on. And I think these are wonderful questions to be asked. And I will say, as was mentioned, I am a clinical lab director and have been for almost 20 years. I co-direct the Central Clinical Lab and the Central Processing Lab at the Mayo Clinic in Rochester. I'm also Vice Chair of Quality for the Department of Lab Medicine and Pathology at the Mayo Clinic. So these topics are, of course, near and dear to my heart.

So I wanted to really reflect on the question being asked in that last slide, which is what is the clinically relevant range of values for an assay. And I think we all think immediately as laboratorians of reference intervals and sometimes called reference ranges, as well. Reference intervals is probably the more contemporary language. And at least in the United States, that is usually the interval of values observed in healthy subjects and often defined as the central 95th percentile of a healthy population.

Now, depending on the analyte, healthy, that description of healthy can be very vague to very, very specific and having a lot of, actually, exclusion criteria surrounding the definition of health. And I thought that the best way to walk through thinking about clinically relevant ranges was to actually pull some patient data from here at Mayo Clinic from my laboratory. And so the first example I'll walk through is TSH, which is thyroid stimulating hormone. And I just pulled a couple of days of data. So the y-axis is not all that relevant. We get roughly 12,000 specimens into my laboratory daily, so volumes are very high. But what we're most interested in, for the purposes of this discussion, is the range of values. And so I've shaded in blue what the reference interval is for TSH. And for TSH, the description of health is extremely specific for what you need, what defines health when it comes to thyroid testing. Clinical practice guidelines will talk about things like no nodules greater than 1 centimeter, no thyroid antibodies, no family history of thyroid disease.

So it's more than just walking in and saying, I feel good today. There's actually a lot to this definition of health. And the standard reference interval, I'm showing reference intervals, of course, for the methods in my lab. And you've already mentioned in the introduction how reference intervals are method specific. They need to also be population specific. So this is very important. But in our lab, it's 0.3 to 4.2. And you'll notice, though, that the spread of data of patient data extends well beyond the reference interval on both ends.

And so that brings up, I think, the second thing that we have to think about when we're talking about a clinically relevant range of values. And that is that reference intervals are only classifying you compared to a healthy reference population. And saying that the central 95th percentile of a healthy population looks like this, and does this patient look similar to that population or different. But it's not an indicator of health and disease. And medical decision points would be, truly, that indicator of either disease or an indicator of risk if we're dealing with a lipid panel.

It might be positive or negative if we're dealing with a qualitative test, or it might be a point at which therapeutic intervention, lifestyle changes, clinical intervention is needed. And going back now to our TSH example, here I have these blue arrows-- are some of what I would consider to be clinical decisions when you're thinking about TSH. And you'll notice that the clinical decision limits are well outside of the reference interval. So I highlighted here this blue arrow. It's usually thought that patients with subclinical hyperthyroidism may have TSHs in this 0.3 to 0.05 range. So this would be important to identify because many of these patients proceed to overt hyperthyroidism. Up to this range from 4.3 to about 10 is generally considered the window of subclinical hypothyroidism, also very important because you would want to assess whether these patients have thyroid antibodies. Are they symptomatic? So I would consider 0.05 and 10 to be clinical decision limits. And then TSH, just a characteristic of a third generation TSH assay, is that it needs to have a limit of quantitation at or below 0.01 milli IUs per liter. So this would mean a coefficient of variation of 20% or less at 0.01 milli IUs per liter.

However, the reason for that requirement is that for biochemical hypothyroidism, this is the threshold at which you'll see

TSH suppressed. And for some other clinical and therapeutic monitoring of TSH, that threshold of 0.01 is also important. So now we have extended our clinically relevant range well outside the reference interval, at least for TSH, between 0.01 and 10. And you'll notice, though, that we do have patients that are less than 0.01, and patients that are greater than 10. And I think this brings up the third characteristic that we need to think about, and that's that deltas in lab results are really important, and that changes over time have meaning. So it may be that you're looking at a reference change value, which is how much change in an analyte actually represents a true physiologic change in that patient. Or it might be that you're measuring response to treatment, and that those changes might be small, in the 20%, to 30%, to 40% decrease or increase range. Or it could be orders of magnitude like it often is with TSH.

So if we go back to that example I've included now, I have my limit of quantitation at the low end, which I would also consider a medical decision limit. But here we also have our analytical measurement range upper limit. So that's AMRUL is 90 for the assay we use in the lab. We have validated up to a times 10 dilution. So we have a reportable range that goes out to the range of 900. Now, for this data pull, the highest patient had a TSH of 40. We certainly do see them higher than that.

And while those are not commonly clinically relevant ranges, what is important in those patients is to know whether this 40 decreases to 4 upon the proper therapeutic intervention, which in most cases, is going to be administration of levothyroxine. So I would argue that even beyond this threshold of 10 at which their therapeutic intervention might occur, a lab needs to be able to reliably differentiate a 40, from a 20, from a 10, from a 4. So hopefully, that gives some context. I do think that the spread and distribution of the frequency of results in patients is really an important component here. And I'm going to go through an additional example. Because when we think of TSH, if TSH is abnormal, the follow up test is free thyroxin. And this is the distribution of serum free thyroxine, or FT4 results. Similar situation here that I've plotted. This was just, I think, two days of data from our laboratory. I have the reference interval highlighted in this light blue, which in our laboratory, is 0.9 to 1.7.

And certainly, the majority of patients are falling within that reference interval where free T4 would be considered normal. But in the case of free T4, the reference interval actually very closely coincides with the medical decision limit. So we certainly have that situation, as well, that if a patient is elevated above 1.7, they're considered biochemically hypothyroid. And if they're below 0.9, they're considered biochemically hypothyroid. Again, our limit of quantitation, our analytical measurement range for this assay goes down to 0.3 with a high end of 7.7 nanograms per deciliter. So you can see, hopefully, on your screens that, while the frequency of results is far lower outside of the reference interval, there are certainly patients out in this range all the way up to a greater than 7.7 nanogram per deciliter result, which in our laboratory, is actually the critical value for free T4.

So coupling in medical decision limits, here we certainly have the reference interval being clinically relevant, but this critical value is also clinically relevant. Clearly, this is considered a medical emergency that needs to be acted on quickly. And I will say, I've been educated even as a long time clinical chemist talking to our endocrinologists in our practice here, because I have thought in the past that if your free T4 is above about 3.5, 3.8, it's high, and high is high. But actually, our clinicians are very interested in monitoring these patients up in this greater than 7.7 range. They wish that the assay went higher because they often have to do even things like therapeutic apheresis to try to lower free T4 in these cases. So this monitoring, this goes into that delta or that trending over time. That monitoring is extremely important in these patients. So it matters if it's a 7.7 or a 6.6, or if it's going from 5.4 to 6, versus 5.4 to 5.

So a lot more to it than just the reference interval. So then I started framing the question because it seemed to me that the clinically relevant range was really the whole range of measurable values. And so I thought, is it better to frame this in what is the clinically irrelevant range of values for an assay, and does such a thing exist. And so I think what would be considered clearly irrelevant would be physiologically improbable results that are still within the analytical measurement range. And what do I mean by that? And do I have an example?

So I chose serum glucose. There could be a lot of assays to choose. But again, I wanted to show you real life data. So this is, again, about 48 hours of serum glucose results. It does not include the glucose tolerance testing or any plasma glucose results. So it's just serum. And if we walk through our logic of how we're going to identify clinically relevant ranges, we have reference intervals both for a random glucose and a fasting glucose. So random is 70 to 140. Fasting is 70 to 100. And again, bulk of the patients within those ranges. But we also have medical decision limits for glucose that are actually diagnostic thresholds. So if a patient has a random serum glucose, plasma glucose greater than 200 milligrams per deciliter along with symptoms, that's actually diagnostic of diabetes. And we have 200 here, and lots of patients that are up above this 200 range. In this data pool, our highest patient was right around a 380 or so milligrams per deciliter. Our critical value for glucose is 400 milligrams per deciliter. We also have a critical low value that is 50 milligrams per deciliter for adults. It's 40 milligrams per deciliter for neonates. And the lowest glucose that we saw in this data pool over two days was a 40 milligram per deciliter. But then we also have the fasting glucose diagnostic criteria for both prediabetes and diabetes. And those are indicated here in purple. So this is the pre-diabetes range. And then anything greater than or equal to 126, this value would be actually diagnostic for diabetes if it's measured, also, by either

a second opportunity or a second test, being hemoglobin A1C.

So now we have a situation where, really, I think that we've shown that patient values actually span this entire range. And if we include critical values as medical decision limits, which they certainly are, we're spanning a range that is 40 milligrams up to 400 milligram per deciliter. And certainly, there are patient results across this entire range. But interestingly, with glucose, our limit of quantitation for this assay is 2 milligrams per deciliter, and our analytical measurement range upper limit is 675. We have validated up to a times 3 dilution. So we get up to-- I think that ends up being 1,300. Don't quote me on that. Should have done that math beforehand. So we have very high measurable range for-- or excuse me. A high reportable range for glucose. And however, how often do we see results up in the 2000, 3000s? Not very often. Often time, those results are actually contamination from IV solutions that contain dextrose. And we have mechanisms to work that out in the laboratory. It becomes a pre-analytical factor.

And if we think about physiologically improbable glucose results, I would say, anything less than 30, roughly, becomes incompatible with life. So certainly, now we have an assay where we still have a very wide range of clinically relevant results, but I would say, between 2 and 30, and maybe above that 400, maybe above 600, become physiologically improbable. And they generally encompass-- and if we start thinking about more analytes, again, I wanted to give a specific example to frame all of this information. But these become the extremes of the measurement ranges. And so possibly, the way to think about this is, what is clinically irrelevant, rather than clinically relevant. There is a caveat here, which is that we, the labs, were still accountable for accuracy within the analytical measurement range, even if it's clinically irrelevant. So it doesn't matter if the span of results is clinically relevant. We still are accountable. And what does that mean? We are accountable for precision across our measuring range for accuracy that our results are the truth. Within that analytical measurement range, we have to confirm linearity and recovery as some of the parameters. We have to prove that the dilutions that expand our reportable range recover appropriately, or if samples are concentrated, that those are recovering appropriately. And then we have to make sure that our reference intervals are method specific, population specific, and have been verified within our own laboratory. But I think there are many other means by which we do this that proficiency testing doesn't need to address all of these things. So we're very accountable to all of these analytical performance characteristics. So when the question comes back to clinically relevant range of values, I think from just my professional experience, and also, wearing the quality hat, and that I think about these things a lot, I think this data driven approach is really important in thinking about who are we serving, the patients we're serving, how are the results used, and that there is more to it than reference intervals. There's actually more to it than just discrete medical decision limits, and that we have to think about that. It's possibly a better approach to determine the clinically irrelevant range of values. I think that helped me frame this. And when we are considering clinically relevant ranges, I think that a good starting point is to look at our data and consider these parameters, which of course, reference intervals, but also, when are these therapeutic interventions made, what are the medical decision limits. And when we have to monitor changes in values over time, what's relevant there, as well?

So thank you for your attention, and I'll turn it back over to the moderators. Thank you.

CLIAC CHAIR: Great. Thank you. That was a great presentation. Really loved the data driven nature of it. Any for the committee before we go to public comments? Any questions for Dr. Baumann? [CLIAC MEMBER]?

CLIAC MEMBER: All right. Thank you so very much for this presentation. And it really, I think, sets the discussion beautifully. One question for the moment, and that is auto dilution. The maximal dynamic range can be expanded by auto dilution. And either in your own practice or you're thinking about proficiency testing, should that tripwire be triggered?

DR. NIKOLA BAUMANN: My gut reaction to that is that we have, again-- this is where I say that there's an accountability for knowing that our dilutions work. And we have that accountability as part of our validation. So I would say no, I don't think that needs to be a threshold. I think the analytical measurement range is the range to challenge. And before we even accept using auto dilution on an analyzer, we are validating that practice and validating that those dilutions recover, that the instrument performs the same as if a human were diluting that sample. So I think my answer would be no, because we're validating the performance of that dilution using a different means.

CLIAC MEMBER: Thank you.

CLIAC CHAIR: So I also wanted to ask a question to help frame the conversation and clarify something, as well. So my understanding is the guidance you're looking for from CLIAC is, for the PT providers, those that are creating the PT programs, there are existing regulations or guidelines that they must meet in order for it to be an acceptable PT program. So and you showed what those regs are. One of them was-- and if you could bring it back up, I just want to clarify. I remember there was being a high and a low plus minus, I think, 10%. Was that of the reference interval, or was that of the AMR? So I don't know if, Angelique or Victor, if you had that can pull that up. It was in the deck.

DR. VICTOR DE JESUS: Yeah. That's 10% of either the lowest or the highest level of the AMR.

CLIAC CHAIR: Of the AMR, not the reference range, not the reference interval. OK. So it sounds like we're already requesting or demanding that the PT providers span the AMR. Certainly, the concept well introduced in terms of the medical decision points. I'm sure that will be part of our conversation. The other scoping question I have for us, is this for all analytes, or only the regulated analytes? What do you want them to be--

MS. ANGELIQUE DAUBERT: Just for the regulated analytes. Sorry, I should have specified that.

CLIAC CHAIR: OK. OK. So, yeah, I think that's the right-- for me, that was just to help scope our conversation and the ask. Go ahead, Victor.

DR. VICTOR DE JESUS: Yeah, I just want to clarify, what I said on the slide was within 10% of the lowest or highest reference value. So yes, you can take that as a AMR.

CLIAC CHAIR: OK. Any other questions for Dr. Baumann? All right. [CLIAC DFO], do we have any public comments?

Public Comments

CLIAC DFO: Yes, we have two public comments. The first will be Dr. Diana Cardona, again, from CAP. And then a second will be Sue Styles will provide a public comment from the American Proficiency Testing Institute, APTI.

CLIAC CHAIR: Excellent. Yeah, let's do it.

DR. DIANA CARDONA: All right. Good afternoon. Yeah, so Diana Cardona again, a practicing pathologist, Vice Chair and Associate Medical Director of Duke Health Clinical Laboratories, here again on behalf of the College of American Pathologists, again, whose mission is to improve people's health by serving patients, pathologists and the public, by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide, and by expanding health equity. The CAP appreciates the opportunity to provide this statement regarding terminology used in CLIA regulation related to proficiency testing or PT. Within the Code of Federal Regulations, the terms clinically relevant range, full range of values, and full range of interpretation that would be expected in patient specimens are all utilized. This variation in terminology invites confusion. We urge the CLIAC to consider this an opportunity to discuss and understand the needs and considerations of laboratory stakeholders to ultimately share a clear vision of the agency's intent regarding revising CLIA's language around range of values.

The CAP supports increased clarity in the range of values for PT. But as we know, the details are what become complicated. Hurdles that must be considered include potential manufacturing limitations, the clinical utility of the test results, assay harmonization, the lack of globally accepted reference intervals, potentially increased costs, and impact on PT performance. Otherwise, PT could inadvertently become problematic exercise with limited value to laboratory participants, and ultimately, our patients. Approximately 500 physician and doctoral scientists with expertise in pathology and laboratory medicine serve on the 29 discipline specific scientific committees within the CAP. In their advisory role, our members review anonymous PT performance data, write scientific discussions when applicable to educate laboratory personnel, and set specifications and targets for the CAP's PT programs. When writing PT specifications, consideration is given to clinically relevant ranges and values, the availability of appropriate material our expert members feel are most important for ensuring appropriate high quality patient care, and compliance with regulatory requirements listed in subpart I. Occasionally, for certain analytes, it's difficult to offer a challenge at the lowest end of the reference range due to manufacturing limitations. Additionally, many routine analytes have negligible clinical significance at low concentrations. For example, aspartate aminotransferases. Our committee members, most of whom serve as laboratory directors, set the specifications for PT samples to emulate real clinical specimens, and that are also relevant to points where medical decisions are made. It is also worth mentioning that it becomes exceedingly difficult to offer an analyte at the low concentration if the regulations do not allow fixed limits with fixed percentage units for that analyte's acceptable performance. It can become problematic to grade those challenges, and could result in an increase in non-consensus or failure rates. In our written comments, we give a couple of detailed examples of PT assays with manufacturing limitations, or that lack clinical utility. We hope that broader, robust discussions with key stakeholders and PT providers will be held prior to advancing proposed regulatory revisions on this important topic. The CAP stands ready to contribute our scientific knowledge and real world expertise at such discussions. And once again, thank you for your time today.

CLIAC CHAIR: Thank you.

CLIAC DFO: And we have lost Sue Styles from API. So if she joins, I will let you know.

CLIAC CHAIR: OK. Is it all right? Should we continue on with the discussion?

CLIAC DFO: Yes, continue on.

Committee Discussion

CLIAC CHAIR: So all right. So, again, I think just to rephrase the scoping, we're being asked to provide some insight as to how do we help define clinically relevant ranges, or, I would say maybe alternatively, potential targets for PT programs of the regulated analytes beyond what the current requirements that were shared with us. And I think that the only quantitative requirement was that plus-minus 10%, or within 10% of the AMR extremes, both low and high. So I'll open it up to the group. Are there any comments, reactions, reflections that you would want to share about the topic in front of us? And Heather, can you put up the guiding questions? Any questions, comments? So I could share what I was thinking in terms of when you're reviewing what the current requirements are. It gently touches upon it, but I think it could benefit from explicitly calling out that, if at all possible, PT program providers, in addition to having the low and the highs, should also have PT events around those clinical or medical decision points. I think that would be very important, and recognizing that those medical decision points could be treat, not no treat, but also, including of the critical values, as well. Obviously, critical values require treatment, just, obviously, different ones. So for me, that was what I felt was missing from the current requirements. I don't know how everyone feels about that. Is the quietness alignment? Confusion? Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I'll maybe admit to a little confusion. I think that one of the things that I heard mentioned was the timing of these things, in other words, the delta. That doesn't seem to be reflected at all in the proficiency testing, yet clinically, that's one of the most essential things that people see. I don't know how we'd do that in PT. It's kind of a challenge. But then the other question I was going to ask about, and this has to do with work that's going on in our lab, is reference intervals are now being determined dynamically for patients. And so how does that play into PT going into the future? I know it's a thorny question, but we all know that these ranges are somewhat artificial when it comes to an individual. So how do we address this in the modern age where we're actually generating these things dynamically for a patient at the time of care?

CLIAC CHAIR: Yeah, it's a good point. And of course, deltas are critically important for patient care. I think in the setting of PT, these are static assessments. You could certainly create a nice story of five PT samples and one-- you could create the story where one's two hours after the initiation of therapy. But I think the delta is not something that could really be addressed in a PT program. And I will also say for the reactive or the varying reference ranges, not only within an organization, but across organization, but across platforms. These PT programs, they basically create a sample of truth, what is the value. Different test systems can give different results. Very commonly seen in, say, liver enzymes, that just different systems create different results. And typically, these PT program providers grade you in your peer group. So the Roche peer group is graded amongst the Roche peer group, and the Abbotts amongst the Abbott peer group. So I think that's also already kind of a company or addressed in how the PT provides their program today.

Public Comments

CLIAC DFO: So Sue Styles is back on. So if we can pause and allow her to do the public comment from APA.

CLIAC CHAIR: Perfect.

MS. SUE STYLES: Hi. Thank you. I'm so sorry for the interruption. My computer did something I've never seen it do before. Mr. Chairman, members of the CLIAC, my name is Sue Styles. I am director of quality and Regulatory Affairs at American Proficiency Institute, API. For over 30 years, API has been one of the nation's largest accredited proficiency testing providers, today serving over 20,000 hospital and physician office laboratories. Thank you for this opportunity to speak with you today. To expand on the API written statement, I have three suggestions for your consideration related to the range of values for proficiency testing samples. One, for a more impactful review of the targets provided, it may be useful for reviewers to know which analytes are best summarized through peer group data. It is reasonable to recommend that proficiency testing providers list up front each analyte for which peer group data is more representative than all participants' data. Simply put, there are two ways to calculate the target value for each analyte tested, all participants means, and peer group means of results generated by similar test methods. 30 plus years ago, the all participants means were written as the default for CLIA, but peer group means were permitted where necessary. And today, peer group means are the default for proficiency testing providers. That was acknowledged in the CLIA wording changes finalized in 2022. To illustrate the difference this makes when reviewing the range of targets provided by a proficiency testing provider, let's look at the example of prothrombin time. It's known that results from different prothrombin time methods are-- can you see the slide? Just wanted to make sure. OK. It's known that the different results are not comparable, and this difference is magnified when testing proficiency testing samples. So this first slide shows the all participant means for all of the 2023 proficiency testing samples from API. When those means were compared to a reference range of 9.4 to 12.5 seconds, from these values, it appears we did not challenge the low end of the reference range. But if the data for one of these samples at 11.0 is reviewed by method, as shown in the next slide, you can see that bias in the all

participants mean, mainly caused by one method. This is the wrong-- I had it colored differently in my other version-- obscures how low the results were for many participants. Two peer group means we're higher than the all participants mean, and that's reagent D and E here. The one in yellow is significantly higher. Three peer group means that up here, these three lowest ones were actually lower than 11, and the lowest one represented half of the participants. So in fact, many participants reported results near the low end of the given reference range, and that's more apparent when the peer group data is reviewed. Our second suggestion is that there should be recognition that proficiency testing results vary from results on patient samples due to matrix effects. Those effects are due to using a manufactured sample because pooled plasma is frequently used. There may be stabilizers or preservatives present, and multiple analytes can be officially targeted in the sample. One type of matrix effect is when substances in a sample other than the intended analyte may affect the quantification of the intended analyte, and that can impact each methodology differently. But those using the same methodology are affected similarly, which adds to the importance of reviewing proficiency test results or targets by peer group. As an example of the effects of pooled materials, in 2022, a leading provider of hematology samples wrote an open letter to proficiency providers on the technical limitations of proficiency samples for white blood cell or WBC differentials. And they stated, quote, proficiency products are manufactured from multiple donors. It is not achievable for WBC differentials in stabilized proficiency products to represent the full range of values expected in patient results. End quote. Finally, to ensure a broad range of targets, it would be helpful if proficiency testing providers were informed of the desired ranges for each analyte a bit further in advance. Currently, the requests for different targets are reviewed toward the end of the annual proficiency testing provider reapproval process. I'm sorry, they're received towards the end of that process. And that allows limited time for us to make any adjustments that would require research and development. In addition, with changes to the reference ranges under discussion, requesting individual PT providers to adjust their targets for the upcoming year, earlier in the current calendar year would also allow an opportunity for feedback on any challenges that might arise from manufactured samples. So on behalf of API, thank you for your consideration of these comments. I would be pleased to answer any questions you might have.

Committee Discussion

CLIAC CHAIR: Thank you very much. OK, let's continue the discussion. Excellent. So questions, comments, reactions? Again, I can propose something to chew on, but I want to see how the committee feels first. OK, well, then I'll propose something. So from what I understand, the questions and the request is-- excuse me. I would envision an ideal PT program to certainly assess the extremes, low and high, as best as possible. And again, what I said it before, it felt like what's missing from the current requirements is the concept of medical decision points. So I'd make a recommendation that the requirements for PT programs be updated to include some degree of concentration around medical decision points. When I say that degree of concentration, using some of the verbiage that was there before, like at least one of them over the years has to be within 10% of either the upper or lower limit. So something along those lines where medical decision points can be tested throughout the PT cycle. And obviously, we don't have to describe it. CMS can just figure that out, figure out what a reasonable cycle would be. In terms of, OK, how do we now decide where these medical decision points are, I would recommend to say, having the PT program providers propose what those medical decision points are, supported by literature that can be evaluated by the PT program. Again, I have no insight into these PT program evaluations. So if what I'm saying is completely bonkers, let me know. And I do want to be very cognizant that sometimes creating these PT programs, as what was just discussed as the extremes, particularly the lows, it's hard to remove something. It's much easier to add something. They're really hard to manufacture. So to give some avenue for the PT program to say we can achieve this 10% of the lower limit because, and an explanation that can be reviewed and assessed. So first, I'll ask [CDC EX OFFICIO]. Is this kind of the feedback that you were looking for? Is this helpful, or are we way off here?

CDC EX OFFICIO: This is all very helpful. That being said, and this is for the committee's consideration. When we discuss the signing specimen challenges around medical decision points, well, how are these medical decision points applicable across the broad range of methods that are out there? We're, for the most part, talking about quantitative measurements here. So it is my opinion that a thorough inclusion of medical decision points essentially personalizes PT challenges to different institutions. And that may be something that may be better addressed by either a sample exchange program or participation in other external quality assurance programs. So that may be difficult to achieve by proficiency testing programs. So I'm not suggesting that that is not a worthwhile activity, and it's certainly something that any laboratory that wants to have high quality testing should consider. But looking at the difficulties of creating sufficient volume of specimen challenges be distributed to many laboratories for all of these analytes presents an incredible logistical challenge, in my opinion. So anyway, I'm going to leave it right there. And [CLIAC MEMBER] has a comment. Over to her.

CLIAC CHAIR: Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: Can you guys hear me?

CLIAC CHAIR: I can.

CLIAC MEMBER: All right. So I was listening to this conversation. I think the medical decision point and having the proficiency provider set that up I think is going to be quite challenging. I'm wondering if the focus should just remain on the analytical performance. And I'm saying that because sometimes, and for me, for example, I'm thinking of viral load testing, where medical decision is going to vary even by patient population. There's no way for a proficiency provider to even set what the medically relevant points are. Sometimes you want really high sensitivity. Sometimes it doesn't matter. But if the focus is just on, is the lab able to analytically pick up this the range of value, that might be where we want to focus. Because I'm concerned that having the medical decision point there might make it almost impossible, given the wide range of PT type that there is out there.

CLIAC CHAIR: Yeah, I think it's a great point. And certainly, [CDC EX OFFICIO] was mentioning it, as well. Because you can imagine a world where if we're going to be so precise with the medical decision point, you have to break down into different manufacturers. And even sometimes, the manufacturers are different methods. And to really target them all, you're basically making PT programs for a near infinite number of systems. And then, of course, you lose your statistical analysis on the back end because your ends are going to be quite low. I kind of view this more as a big picture, to use the phrase I used last time. It's the rising tide. Right now, it may not be in a particular test system. It may be right on the medical decision point for test system A, and slightly off for test system B, or maybe even significantly off for test and B. But by declaring this inclusion of medical decision points in the requirements for PT programs, it's in the ballpark. And it's still rising the tide of quality, even if for each individual test system, it is not exactly on the medical decision point.
So for me, I'm more comfortable with just an imperfect improvement than I agree with you, I think making it perfect, the whole system falls apart. So sorry. Is your hand still up? Did you have something else to say? OK, I don't know. And, [CDC EX OFFICIO], I saw your hand up. I don't know if you pulled it down.

CLIAC MEMBER: Sorry. I'm going to lower it.

CDC EX OFFICIO: No, same here. I hit the wrong button. My apologies.

CLIAC CHAIR: [CLIAC MEMBER].

CLIAC MEMBER: I'd like to weigh in on this, because I think you make a very good point. You can't consider everything in this decision making process. But what we're recommending that it be updated to consider some of the medical decision points when possible. But we don't want to make it so cumbersome that the manufacturers of the PT materials have to invest a lot more time and money into this, because it's going to make it a lot harder for us as purchasers of these supplies. So I think a midpoint is desirable here because we see a need. A matrix approach, rather than just a statistical approach, has a great deal of value to it. But let's not get too much into the weeds where they're actually designer panels.

CLIAC CHAIR: Any other questions or comments? Any negative reactions to this recommendation? Does someone feel like it's a nonstarter?

CLIAC MEMBER: I just had a quick question.

CLIAC CHAIR: Go ahead.

CLIAC MEMBER: Thank you. I just was wondering, with there be so many different manufacturers, how, for example, if a patient has a test in one state and they use a different one, how do you account for the differences in the variability of those tests in order to make a decision as a clinician if there's a big discrepancy within those? Is there a certain adjustment factor that we have, let's say, for manufacturer X machine, that the test was run in a lab, versus in a different one to make, I guess, to adjust for those differences?

CLIAC CHAIR: In the PT programs, you're saying?

CLIAC MEMBER: Yes, as an example. Yeah.

CLIAC CHAIR: Usually, the total population that participated in the PT is broken down into their peer groups. So you'll compare Abbott method A to Abbott method A. You're not comparing it to Abbott A to Roche B. So that's how they account for some of the variations in the test systems. You're comparing amongst your peer group.

CLIAC MEMBER: Thank you.

CLIAC CHAIR: [CLIAC MEMBER]?

CLIAC MEMBER: Yeah, this is an interesting discussion. However, I kind of reacted to your comment, [CLIAC CHAIR]. Does anybody have any negative reactions to this? I sort of do. Are we prescribing to the programs what they are

supposed to do? And why don't customers prescribe that? Why don't the customers put pressure on these PT programs? Is this a role that we really need to take on?

CLIAC CHAIR: Yeah, and [CDC EX OFFICIO], keep me honest here. The PT program providers actually have to be approved by CMS. And so every year, they have to submit-- I don't know what data they submit. But they have to be approved. They have to meet the requirements that are lower on this document that are set by CMS. So CMS is now asking us, we have this. How do we define what's clinically relevant from a PT perspective? They've already covered the extremes of the AMR. And so how else could we provide clinically relevant ranges? And that was why the proposal of the medical decision points to be included. But yeah, it's more than just the customer. They have to get approved by CMS. [CDC EX OFFICIO], did I represent that properly?

CDC EX OFFICIO: Well, program, yes. PT providers have to be approved by CMS, and I'll defer to [CMS EX OFFICIO] on that specific process.

CLIAC CHAIR: I don't know. Yeah, sorry. I can't see [CMS EX OFFICIO]. [CLIAC MEMBER], you have a hand up?

CLIAC MEMBER: Yeah, I guess I have a clarifying question. I think there was a comment earlier that this-- is this only for regulated analytes, or is this for all?

CLIAC CHAIR: Yeah, the scope is for regulated.

CLIAC MEMBER: OK, because I guess I'm coming from my own little niche where I'm not really doing a lot of regulated analytes. My initial comment for, I guess, outside of that, just even getting consensus on what's medically important range is difficult for a lot of tests and isn't very well established.

CLIAC CHAIR: Yep. And [CMS EX OFFICIO], I was able to find you. I didn't know if you were commenting before or not.

CMS EX OFFICIO: No, I was just saying that I didn't think it was necessary to go through the process of approving proficiency testing organizations for this discussion. We do approve them.

CLIAC CHAIR: OK. Any other comments or reactions? Again, particularly the negative ones. Because obviously, you know where we're going to go next. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I guess my question is the feasibility, really. Because the way it professionally works is that you have to have a sample that you can allocate into thousands of little aliquots and send it to. And we already know that there are issues with matrix effect. But when we talk about decision points, are we saying, try to get it at the border of reference ranges? Because CLIA requires us to verify and adapt reference ranges to our patient population. So how do you make that laser incision to where you want to get a sample that has a known quantity that is close to somebody's reference range? It won't be everybody's reference range because everybody's different enough that it does-- so I guess that's my head scratcher is, how would this be achievable. I guess it might be easier for certain things such as, definitely, sodium, maybe, and potassium. But once you get into things like AST and ALT, I don't know how this would be actually be feasible from a technical point of view.

CLIAC CHAIR: Yeah, I think that's why the recommendation was giving that degree of flexibility, as well, recognizing manufacturing challenges and all of that. And again, this would be stating that, when possible, medical decision points should be tested in PT programs. The program provider can define those medical decision points supported by literature that can be potentially reviewed and agreed upon. But of course, we recognize it's not going to work for all systems. So I guess, said otherwise, I guess we have two choices. We could make a recommendation something like this, or say that the current system is-- we think the current system is fine the way it is and have no recommendation. Yeah, but I totally appreciate everyone's comments of the imperfection of this recommendation. It won't be perfect. The question is, do we feel like it will-- at least targeting close to those medical decision points. Is that increasing the overall quality of the United States or test system, laboratory systems or not contributing anything? I would say, if we think it would contribute to the overall quality, I would propose moving forward with it. If not, if it's neutral or negative, obviously not. [CLIAC MEMBER], I see your hand up again.

CLIAC MEMBER: Yes, I was reacting to [CLIAC MEMBER] comment about the reference intervals being used as the sole way to interpret this. And as Dr. Baumann correctly pointed out in her nice talk with those examples, there's other decision points, other decision concentrations for these analytes that are used and ought to be used by clinicians, and therefore, in PT programs. Because we need to assess our methods, and the proficiency testing exercise should assess our methods at these different decision points, like for glucose. It's not enough to test at 126 and leave it at that. There are patients up in the 200 to 400 range. We need to test in that range, as well, and below, like about 50, like Dr. Baumann said.

CLIAC CHAIR: Absolutely. Yeah, I think all those would fall into the category of medical decision points.

CLIAC MEMBER: Exactly. Is that not the AMR?

CLIAC CHAIR: So yeah, there's AMR, but then there are points in between, like hemoglobin A1C. You can test the extremes, but they're the decision points of what defines prediabetes and diabetes. So in addition to the extremes, where are the ones, where are the decision points in between? Not all analytes may have a medical decision point. Right? Some may, some won't. This is at least providing additional guidance to PT providers, if applicable, target a medical decision point at some frequency once a year, every other year. Rotate through the various medical decision points if there are multiple. More in a particular analyte?

CLIAC MEMBER: I've been struggling with this concept of medical decision point through this whole discussion, because going back to what [CLIAC MEMBER] said earlier, the medical decision points can vary extraordinarily widely between age and condition that a patient might have. Pediatric oncology versus adult endocrinology, for example, are very different patient domains. And to ask laboratories to anticipate the medical decision points of what likely is to be a very diverse clientele, patient population that they serve unless they're a niche laboratory, I think is asking for discernment that is beyond the requirement of an earlier comment, which was, well, what is the analytical dynamic range, and what is the accuracy of it. And so the reason I struggle is the concept of medical decision points. And this is not critical values as such, which themselves can be debated for, whether critical, or hyper critical, which is a term that makes me flinch, can be defined on the basis of evidence. It's something that a laboratory cannot do in isolation. It has to be done in working with clinical colleagues. And the structure for doing that, to me, is-- you could argue it's beyond what CLIAC should be paying attention to. So while on the one hand, I consider it a meritorious concept, putting medical decision points into practice, to me, is a very difficult tactical exercise for a laboratory to engage in.

CLIAC CHAIR: Yeah, I think the comments are well taken. To be clear, this is guidance or requirements not of the lab, but of the PT provider, the manufacturer of the PT. The requirement today states for the 29 regulator-- I think it's 29 still-- 29 regulated analytes, is the only guidance they have is you need to be within 10% of the lower range, within 10% of the high range. All of their other PT challenges that they manufacture, they could put it anywhere in the analytical measurement range. This would simply be saying, additional guidance in addition to the extremes, also, when applicable, target those medical decision points. And Some of them will be prescribed. They're standardized assets.

CLIAC MEMBER: They're established guidelines for what constitute out of, use the term, medical decision points.

CLIAC CHAIR: Right. So it's simply giving them more guidance to target those medical decision points, recognizing the variability across assays, and recognizing it won't be precise for all of them. But again, it's just more guidance and manufacturing. They have to make 15 analytes, 15 tubes a year, two of them have to be at the extremes, giving them more guidance as to what to do with the other 13.

CLIAC DFO: But I also want to clarify something, that this that [CDC EX OFFICIO] presented is not a clear regulatory requirement. This is something that the CDC does as part of their program review and provides the report back to CMS to utilize when they're doing their approval of the PT programs. So this is just what we have at CDC decided to use. In no way, shape, or form is that currently in the regulations for what PT programs must do.

CLIAC CHAIR: OK, does that open the door for a recommendation of including that as a requirement? [CLIAC DFO]?

CLIAC DFO: Yes, it could. If it's felt that there's more specificity needed in the regulations, we could do that.

CLIAC CHAIR: OK, so I'll rephrase, reframe the conversation, especially in light of that. So it sounds like there is no requirement of PT providers to select or manufacture their PT challenges. There are no requirements. They could do anything. They could just do pooled plasma 15 times in a year. And wherever it lies, it lies. So we can say that that's OK, we're content with that, or we could provide a recommendation to require that PT providers test the analytical measurement range extremes and/or medical decision points. So really, the question really comes down to, are we satisfied with the status quo, which is no specific requirements of where the analytes or where the PT challenges should lie within the AMR, or do we want to provide some. [CLIAC MEMBER]?

CLIAC MEMBER: I actually like the idea of enshrining these requirements that [CLIAC DFO] just had highlighted. Because I think reading through them, they are actually realistic, in terms of that it should reflect the range of what we will get into in a patient. I think trying to pinpoint exact values along so-called decision points, I'm not sure how realistic that is. And then you get into the question of the albumin, where the literature is full of national guidelines for albumin. That doesn't really tell you which method is. It bromocresol green, or bromocresol purple? And they're 30% different. And we're not harmonized. And so if there is no clinical decision point for so-called bromocre-- I'm probably getting it exact opposite. But there might be one for purple, but not for green. So what do we do then?

CLIAC CHAIR: So I'm hearing support for the extremes. I'm hearing cautious. I wouldn't even say cautious part. I'm hearing cautious, caution for medical decision points. I do want to reflect back because maybe I'm hearing this as an anxiety with calling out those medical decision points, is the PT will be assigned a value, and different methods will give different values. And I want to stress again the grade, how they're graded by peer groups. So if the decision point was, say, 12, whatever test, whatever units, and in Abbott instrument, the peer group is 10, it's not like those labs are going to fail because the decision point was 12. You're graded amongst your peer group, so you're not going to fail. Labs won't necessarily be at risk here. Again, we're providing guidance to PT programs to at least target around the area of the medical decision points. I feel like we're getting caught in the precision of this when we're not looking for precision. This is guidance of where to manufacture PT analytes or your PT challenges. So I know I keep repeating myself, and obviously, because I keep repeating myself, I'm mentioning it. Obviously, I'm an advocate for it, but I'm not feeling the same advocacy from the rest of the group. If the support is not there, we can forget it. But I just want to make sure that we understand what is being asked of us so we can decide whether the support is there or not. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I think we should just not let perfection be the enemy of good here. And I support what you're saying. I don't think it's particularly restrictive. I don't think that what is being stated here is restrictive. I think it is leaving an opening for there to be some flexibility.

CLIAC CHAIR: Yeah, thank you. Yeah, I agree with the flexibility here. And again, for the PT program providers who may flinch at sometimes the real manufacturing challenges of getting to these points, I think explaining why you can't get to those, why you can't create a challenge at some particular range should be sufficient to meet that requirement. Because some of these things will be very challenging, if not impossible, to meaningfully manufacture. [CLIAC MEMBER]?

CLIAC MEMBER: I guess my question is, for the 15 challenges, I know they have to be one close to the high, one close to the low. Do we know what those other 13 challenges look like? Are they within that range of what would be medical decision points, or do we not know anything about them? So what you said, Jordan, are they the same value of 20 for the other 13, let's say? And does that matter?

CLIAC CHAIR: Yeah, that's the ask of us. As of today, there's no requirement for them to-- first of all right now, today--

CLIAC MEMBER: But if they can do the low and they can do the high, then why would it not be that they could do in between? I guess that's my question. Are we making it more complicated than what it already is?

CLIAC CHAIR: I do think the manufacturing challenges are going to be the low and the highs, not so much in the middle, to your point. But yeah, as of today, there's no guidance. There's no true requirement of low, high or medical decision point. And that's the ask of us is, do we want to provide some requirements or recommend some requirements to improve the overall quality?

CLIAC MEMBER: Could we just say more variation within the limit ranges?

CLIAC CHAIR: Yeah, we could.

CLIAC MEMBER: So that we don't get too caught up on the medical range, just that there is some variation that can be detected. But again, I don't know what's currently done with these analytes because I've never tested the chemistry analytes or hematology analytes.

CLIAC CHAIR: Yeah, I think variation is certainly helpful and it's what we would want. The word variation alone is not particularly helpful. You'd have to put some parameters around that. 13, 13.1, 13.2. 12.9. Is that variation if your AMR is 0 to 100? Probably not. OK. [CLIAC MEMBER]?

CLIAC MEMBER: I actually think there might be some good that comes out of this, because I think that we as a profession have not done a good job in terms of conveying just how much variation there truly is between, not just interpatient variation, but between the different platforms. And I still have conversations on a weekly basis with conditions or with pharmacists who are shocked that they have to adjust their guidelines now that we've switched to a different chemistry analyzer. So maybe by illustrating that the decision points are different for different platforms, and somehow broadcasting that, might make a difference, that you just can't turn everything on the same line and treat everything the same way.

CLIAC CHAIR: [SUBJECT 15]? And [SUBJECT 15], is your hand still up, because you have a question? Go ahead, [SUBJECT 15].

CLIAC MEMBER: Yeah, so that's a good point. But manufacturers shouldn't have any trouble coming up with the medical

decision points and assays that work at those points. And therefore, the proficiency testing providers ought to be able to come up with concentrations around those ranges.

CLIAC CHAIR: Yeah, no. Yeah, I agree. Go ahead, [CDC EX OFFICIO].

CDC EX OFFICIO: I appreciate that, and I would like to provide, perhaps, a little bit of perspective as to the development of proficiency testing materials. I spent many years of my career working in a proficiency testing program, and the development of materials with low levels of some analytes can be incredibly difficult. And oftentimes, we accomplish that by using, for example, charcoal stripped serum, which essentially, just gets rid of everything in there. That in and of itself creates a significant matrix effects for other analytes. So while, technically, proficiency testing programs may be able to actually create these kinds of materials, unless they're properly vetted by different methods, different sites, et cetera, it may become an incredibly, incredibly burdensome activity for proficiency testing providers. And another thing to consider is that sometimes when you have these highly manipulated specimens-- and I'm going to give the example of dry blood spots, which is what I used to do-- they end up looking different. And as we all know, PT specimens need to be processed, just like any regular specimen. So if you can spot something right away visually, that's sort of tipping things off, if you will. So there's no perfect solution here. I realize that. But I think for us here at CDC, a discussion about whether that 10% of the high and of the low is an appropriate metric that we should be looking at for our analysis of programs, I think that conversation would be very, very useful to us here at CDC. Over.

CLIAC CHAIR: Yeah, thank you. I want to make sure that's that challenge is represented in the way of flexibility. So in terms of slight or minor wordsmithing of the recommendations so far, as applicable or if possible, I want to make sure that sometimes it is almost impossible to make these samples. And I don't want to throw the baby out with the bathwater here. We need these PT programs, and we can't have them all the program providers all fail because they're trying to create something that can't be created without significant matrix effects, and all of that. But again, as of today, PT program providers have no goalposts to target. They have nothing to target. They can just create samples. This is saying, when possible, here are the goalposts. High, low medical decision points. So we've nine minutes left, or, actually, no, maybe a little bit more. 14 minutes left in the conversation. I still sense angst, confusion about this. And again, I like the distillation of right now, there's no goalposts, and we're just providing guideline goalposts here. Recognizing, of course, what we're saying, we're making the recommendation. And the agencies then have to take it under consideration. There'll be, I assume, engagement with stakeholders to figure out the feasibility and other things. So we are not the final word here. We're kind of just the ones that are kicking off the conversation through the recommendation. Yeah, I want to try and kind of push towards either agreeing to this recommendation or killing it. So I want to ask the question, how do you feel about this recommendation? Any kind of refinements that you want to it, and things like that? Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I think I could support it enthusiastically if we drop the word medical decision point. Because I think, for me, the main thing about that is that it implies that there is a medical decision point for assays. And really, it's all about the clinical picture and everything like that. Going back to the requirements below, could we just tweak it a little bit, where we say that cover full ranges, including those that might be medically significant? That way, I think it's the word point that gets, causes me anxiety. Some things are appropriate, like, I guess, D-dimer, 0.5 for certain assays, saying the probability of DVT. But I think that boiling it down all to certain values.

CLIAC CHAIR: Yeah, I think it's a fair modification. I like it because, for me, the spirit is, I want you to target things around the values that are clinically meaningful. If the word point implies a degree of precision that is inappropriate here, I absolutely support that, meaning I absolutely support removing it, because precision here is not the was not the intent. Mary?

CLIAC MEMBER: Here we go. Just, something that comes to mind is, one of the examples was hemoglobin A1C, and pre-diabetes, and diabetes, and so on. And the pharmaceutical companies follow those religiously for the medications that they'll cover. It'd certainly reduce diabetes if they made Mounjaro and Ozempic available to those people with prediabetes. So there could be a larger impact by not. At least calling out some of these numbers. And then if you call them out, does the lab have to be able to measure them properly? I just think there's medical decision making, and then there's also medical insurance availability of medications that's predicated on some of these values.

CLIAC CHAIR: Yeah, I agree. [CLIAC MEMBER]?

CLIAC MEMBER: A different way to get it, the concept that we're not talking about points, is the fact that even dynamic change within the reference range can constitute medically actionable data, for example, a rising creatinine through the normal range in a elderly person who has limited muscle mass as a sign of loss of kidney function. Something that was said right at the top of our conversation with the presentation is, what is medically and physiologically relevant, as opposed to just trying to span the analytic range, going back to [CDC EX OFFICIO] comments about, very low may not be medically and physiologically relevant. So an alternative is to use the words within the dynamic range of medical and physiologic relevance. Again, that is a judgment call, but I think it does get at something that this conversation has been

doing over its length, which is, what's meaningful. And my version of that is, what is medically and physiologically relevant, as opposed to analytically valid at extremes. And to be honest with you, that was the genesis of my comment, my question about auto dilution. Because if a glucose is 400 or above, do we dilute to find out if it's 500 or 600? Or serum transaminases. How high do we go before we dilute and try to figure out what's really there?

CLIAC CHAIR: OK. So we have--

CLIAC MEMBER: It is an option.

CLIAC CHAIR: So we have three versions up here and a few minutes left. Let me quickly read through them. OK. Just as somewhat of chair's prerogative to make this a little easier, I would recommend to just getting rid of option one. If there are challenges with the specificity of points, let's just get rid of it. To be honest, I think option number two covers it just as well. I still do struggle with that comment of dynamic range because, again, these are PT, not patient samples. And there's no dynamism here. This is a sample with one result.

CLIAC MEMBER: Yeah, and I did not say the dynamic range. I just said range. Nor am I saying that my recommendation is the preferred one. It is a recommendation.

CLIAC CHAIR: So the way I'm reading the difference between option two and option three, option two says PTs should span the AMR and touch upon the ranges that are medically significant. Option three is just saying those that are medically significant. So I think as a PT, when we're trying to challenge our test systems to see as a quality control tool, as PT is, or a quality assurance tool, I would say we need to do both. Test the system at its extremes, as well as those medically significant ranges. So if all right with the group, I would recommend reducing this down to option two. [CLIAC MEMBER], you have a comment?

CLIAC MEMBER: Yeah, I'm going to agree with that. And also, the option, the language doesn't include concentrations. I think we should-- I'm not seeing the thing. There it is. OK. Let's see. Include consideration for analytical measurement ranges, including those concentrations or quantities that may be medically significant.

CLIAC MEMBER: Values?

CLIAC MEMBER: Values? Yeah, you get my idea. But just leaving it undefined there is not good.

CLIAC MEMBER: And I like medically relevant better than significant. Significant seems to box it a little bit more.

CLIAC CHAIR: OK. All righty. I think we are getting close.

CLIAC MEMBER: It takes a village.

CLIAC CHAIR: Questions, comments on the recommendation we have right now? We have five minutes left. So questions, comments, and then I'll ask for a motion and beyond. Hearing none. Do we have a motion?

CLIAC MEMBER: I'll move. Passage of this recommendation.

CLIAC CHAIR: Excellent. OK. All those in favor, please raise your virtual hand. We have a majority. Thank you. The recommendation passes. Probably don't have time to discuss anything else in greater depth, although, to be honest, I feel like we actually covered it in terms of what the ask was of us. We're supposed to go to, what, 2:15 Eastern time. We have five extra minutes. I would propose giving you those five extra minutes for your lunch break. So why don't we take a break now? We'll come back at

CLIAC MEMBER: 3:15.

CLIAC CHAIR: Maybe we should come back at 3:15.

CLIAC DFO: 3:15 Eastern time.

CLIAC CHAIR: We'll come back at 3:15 Eastern time. Thank you very much.

CLIAC MEMBER: All right.

CLIAC MEMBER: Thanks.

Utilization of Remote Technology for Competency Assessments

Introduction to Topic
Gregg S. Brandush, RN, JD, CMS Ex Officio

CLIAC DFO: We can go ahead and get started, [CLIAC CHAIR].

CLIAC CHAIR: All righty. All right. Welcome back, everyone. Hopefully you enjoyed your lunch break. So we're going to close today with the topic of utilization of remote technology for competency assessments. We're going to start with an introduction by Mr. Gregg Brandush, the Director of the Division of Clinical Laboratory Improvement and Quality at CMS, followed by a presentation on leveraging technology for remote assessments by Ms. Michele Klawitter, Ms. Andrea Noon and Mr. Richard Redmond from the American Red Cross. After the presentations, of course, we'll have time for public comments, as well as committee discussion. So I will turn it over to Gregg to kick us off.

MR. GREGG BRANDUSH: Thank you very much. We made the last topic, everyone. Really, a great meeting. This has been outstanding. All right. So this is a topic that we've talked about in various incarnations over the last few years. And I want to start with our historical view of this issue. So we took a poll and asked about people's reception to the idea of allowing virtual competency assessments in clinical laboratories. And we first started with our state agencies. So 71% of them were not in favor of virtual competency.

We talked to our CMS locations. 75% of them were not in favor of this. We talked to the accrediting organizations. 50/50 there. And the reason of support for opposition is that the competency assessment is a single most frequently cited deficiency in CLIA surveys. So you could see we're very change averse group. But just because we're change averse doesn't mean we need to close our minds to emerging technology and how things can be different. And one of the things that I'm concerned with is the citation support that we like to use.

So there's a competency assessment. It was cited in 19% of laboratories cited. It's the standard level, but still the highest level of citation we have for any of the standards. And a government trap is to reach a conclusion and then try to find data to support that conclusion. And that's something I think we may be falling into here. So the citation that we rely on, saying it's number one, really, is a procedure regulation. It states that laboratories must follow written procedures to assess employees and consultant competency.

There are two regulations that require that direct observation, and those don't appear in the 10 most cited list. So it really begs the question that if we were open to emerging technologies and things that enhance or add to our ability to assess our staff, would that ultimately lead to improved quality and safer patient care? And along these lines, and this is really what is the driver of this whole discussion today, the Red Cross recently reached out to us, and they offered a demonstration of a virtual competency model that they believe will reduce costs and improve the quality of competency assessments. And we're going to have a demonstration of that in a little bit.

Before we get to that, though, I want to go over the current regulations so we have an idea of what that is, and then pose some questions for the group. The current regulations are-- there's really two, and the language is the same. They apply to both the technical consultant and the technical supervisor. And the two regulations that you see there 1413, 1451, these require direct observations of routine patient test performance, including patient preparation, if applicable, specimen handling, processing, testing, and performance of instrument maintenance and function tests. And the direct observations portion of that, CMS has defined as meaning in-person observation. One of the things that is a nice, I guess, flexibility that we have in this discussion is, I don't believe this is going-- if we decide this is something we want to embrace and do, I don't believe this is going to require any regulatory change. We can, through our interpretive guidance, expand and broaden the definition of direct observation. So I don't believe we need to go through notice and comment on this because it actually would reduce the burden along the labs, or among the labs. So these are the questions that we would like.

So we would like to know if CLIAC would recommend greater flexibility in regulatory interpretation to allow for virtual competency assessments in the laboratory setting. What's the risk of losing direct in-person observation? So how important are background noise, odors, other activities to a competency assessment? What are the recommended limits of a virtual competency? Should we have guidelines and requirements for specific instrumentation and capabilities, like the product that can be demonstrated? Because, clearly, there's a line somewhere. We don't want somebody holding up a laptop saying, OK, this is my virtual competency, versus a really sophisticated piece of equipment. Should there be workload limits on the number of people who can be assessed in a given day? Again, we want to get away from a competency mill where somebody is doing this 16 hours a day, one after another. Should we create on-site regulatory requirements for technical supervisors and technical consultants if we do away with this particular one? Should this be test specific? And what are the benefits of such a flexibility? So those are some of the considerations for us in the discussion that will follow. And Jordan, I will turn it back over to you.

CLIAC CHAIR: Excellent. Thank you so much for that framing of the discussion. At this point, we could roll right into it and turn it over to our speakers. I don't know who's kicking us off, but we have—

Leveraging Technology for Remote Assessments
Michele Klawitter
Andrea Noon
Richard Redman

MS. MICHELE KLAWITTER: That's me, Michele. Give me just one second. I'm going to share my desktop here.

CLIAC CHAIR: Sure, sounds good.

MS. MICHELE KLAWITTER: Great. Let's see.

CLIAC CHAIR: Just so you know, we're seeing a beautiful background, just not the presentation.

MS. MICHELE KLAWITTER: Are you? OK, great. How about now?

CLIAC CHAIR: Now, yeah, we're seeing-- Yeah, so now we see your-- yep, you're doing it.

MS. MICHELE KLAWITTER: Excellent.

CLIAC CHAIR: Perfect.

MS. MICHELE KLAWITTER: OK, great. Well, good afternoon, everyone. We are very excited to be here today. We really Thank the CDC and CMS for allowing us to share this information with you about how we would like to utilize remote technology for competency assessments. Just to introduce myself, I'm Michele Klawitter. I'm the Vice President of Quality Assurance here at the Red Cross in Biomedical Services. And I'm specifically responsible for our quality management systems, and one of those being our design and development of our training programs. And with me here today, I have Andrea Noon. Andrea.

CLIAC CHAIR: I'm sorry. I'm sorry to interrupt. I don't know if everyone else is seeing. Does everyone else see that square or rectangle that's blocking the view? Yeah. Michelle, I don't know If you maybe want to close out of that, and then reopen it. I don't know if you see that, but there's a rectangle in the lower right hand side that's obscuring part of the presentation.

CLIAC MEMBER: Yeah, I see that as well, Jordan.

CLIAC Member: Yeah, it's still there.

CLIAC CHAIR: Yeah, it's still there. OK, hopefully, it won't cover too much. You could just continue.

MS. MICHELE KLAWITTER: I'm sorry. I could go to a different-- I'm not sure what I can do.

CLIAC CHAIR: OK, don't worry. If there's not a quick and easy fix, don't worry about it. It's not that bad, but if there was an easy fix--

MS. MICHELE KLAWITTER: OK. I apologize. OK, I was introducing Andrea. She is my operational and process partner. She is our director of training strategy for the Red Cross. And Andrea has been instrumental in our journey to modernize our training programs over the last four years. And so she's going to share with you-- she's really our internal expert, and she's going to share with you today information about that journey. And part of that journey has been the use of technology. So we're going to talk specifically about this wearable technology. And I'm also happy to introduce Richard Redmond, who is with Computer Generated Solutions, which is a global company that we have partnered with to design and deliver innovative training programs, new modernized training programs for our staff across the American Red Cross. And we've been partnering with CGS since 2020, so we're happy to have him with us today. OK, so just quickly, these are the things we're going to cover. We'll talk about our objective. Andrea will talk about our Red Cross journey. Richard will jump in and talk to us about the actual considerations for the technology and some of the benefits of technology, which I think will be of interest to you as you listen for-- Mr. Brandush just mentioned that not all technology is the same, and I think you'll see that with Richard's presentation. Andrea will talk to us about the advantages of leveraging this type of technology. And I'll wrap us up with some common questions and concerns that we have learned along the way.

So just as Mr. Brandush just said, first of all, we appreciate the ability to come here and talk about this. But the CFR requires direct observation. And currently, CMS defines direct as in-person. And the Red Cross would like to share with you the successful use of technologies that we've had in our operations to, hopefully, further this conversation, because we would like to employ this type of technology in our competency assessments. And so with that, I'm going to run the video. And I hope that the video doesn't get blocked by whatever you guys are seeing. How's it looking?

CLIAC CHAIR: Should be all right. It's still there, but it should be OK.
[MUSIC PLAYING]

NARRATOR: At American Red Cross, we aspire to the highest standard of regulatory compliance, and we're investigating several innovative technologies to help us do so. The Realwear Navigator 520 is purposefully designed for use in industrial and biomedical manufacturing environments. The 520 is an internet connected wearable tablet, enabling completely hands free work without interfering with the work environment, facilitating supportive mentorship as part of training, as well as observation during assessments. Voice recognition technology allows the user to control the 520 without having to touch the device or look away from their work. The 520 is fully compatible with PPE and can be cleaned to high sanitization standards without damaging the device. It supports unique pin authentication, ensuring the identity of each individual guaranteeing the right person is being observed every time. The integrated microphone array features active noise cancelation and voice isolation, so communication is always clear. Remote observers have a better view of a staff member's activity, thanks to the first person viewpoint, ability to zoom in, and a built in flashlight for low light environments. Unintended distractions that can occur during shoulder-to-shoulder assessments are reduced, leading to less workplace disruption. So with regulatory compliance as our highest priority, we invite you to join us in a conversation to learn more about this innovative hands free technology at American Red Cross.
[MUSIC PLAYING]

MS. ANDREA NOON: Good afternoon, everybody. As Michelle pulls our slides back up, I wanted to just say, hello, my name is Andrea Noon. As she mentioned, I'm the Director of Training Strategy. We're really excited to be here today. And we'll start by telling you a little bit about the investments that we've made at the Red Cross over the past four years to really modernize our training programs for our staff in our collections, supply chain, and service delivery departments. We've been able to save our organizations significant expense by redesigning how we deliver training to our more than 3,000 new hires in these departments annually.

We have partnered with computer generated solutions, as she said, to redesign the training into a technology enabled blended learning program. This new design delivers best in class training that really allows us to work with our new hires, increase their knowledge retention and skill development for those new staff. The blended learning model that we've developed incorporates the various training modalities and the delivery modalities that you see here on the screen. And through this blended learning design, we were able to reduce the time that our staff spend in training, while maintaining successful quality KPIs.

The strategic approach not only reduces the expenses and overcomes the constraints that we had previously in our training programs with in-person delivery, but ultimately, improves the overall training experience for our workforce. So today, we'll focus our discussion on the assisted reality technology that we had tested as part of our project, and are just now starting to use in our manufacturing and distribution areas within the new staff training program, and would like to have it considered to expand into our laboratories for assessments. So I'd like to introduce Richard Redmond from CGS to share more about the various technologies and considerations for our specific use cases.

MR. RICHARD REDMOND: Thanks very much, Andrea. And it's a pleasure to present to you all this afternoon or this morning, wherever you may be. One of the key things that's really important in an approach that, in partnership with American Red Cross, that CGS always takes is, whenever we're looking at making improvements using technology, it's really not so much about the technology, but how we use the technology to improve the processes to make for a more resilient and robust competency assessment process in this particular instance, and obviously, also, in terms of training and other applications of technologies for learning and development.

So in looking at the sea of technologies, there really are a wide, wide range of technologies that could theoretically be used for virtualizing something like competency assessment, for example, from camcorders to smart glasses, and so on and so forth. And one of the key things that we look at in using technology across industries, regulated and nonregulated, is what's the right technology for the use case for the type of challenge that we're trying to overcome, or the process improvement that we're trying to achieve.

And we really narrowed in on wearable devices, in particular. And a variety of wearable devices we investigated to determine whether they would be suitable for doing virtual competency assessment. And one that we, ultimately, landed on through our process was head mounted assisted reality devices, and in this case, the Realwear 520 device. So how we landed there, if you don't mind moving to the next slide, was through a very careful consideration across a range of

different categories of attributes and factors.

So for instance, with a wearable device, we looked at and actually did a comparison between wearable glasses, like the Ray-Ban and Google Glass to other forms of wearables, like the head mounted tablet, the Realwear device, which ultimately, is what Red Cross selected. But the key factors in terms of form factor was the wear ability and hands-free. You may recall from the video the reference to the requirement to be able to control the device without physically having to manipulate something like a smartphone or the device itself. So using, not only that it's wearable, but that the hands free operation of the device using voice recognition.

Obviously, compatibility with PPE was important. The device itself, must not interfere with the actual work tasks that are being assessed, the regulated tasks, and in addition to that, not introducing other human contamination into the environment itself, as in disrupting others who are concentrating on their work, and also, of course, the ability to withstand fairly rigorous cleaning standards. So that's just in terms of form factor. But functionality, like key elements of functionality, the quality of the camera video feed.

So for instance, the quality of something that you might capture on a smartphone, and then broadcast using the Zoom technology, for instance, which is really optimized for the human face, is not necessarily the right software technology solution for being able to see the fine details on a form or a lookup table, or charts that are used in clinical testing. So the quality of that image, being able to actually pick up the finer details, so the quality of the camera being very important to achieving that. But also, and I think it was mentioned mention in some of the questions or considerations, the ability to be able to, either isolate sound when you want voice isolation, but also, the ability to turn that off so that you can hear remotely, maybe some of the other noises or environmental considerations. The ability of the camera to be adjustable and configurable. The ability for the device and the software to have the ability to use optical zoom, so that you're not asking the wearer to put themselves in an ergonomically awkward position that they would not normally be in, carrying out the tasks and the clinical lab environment. So that being a very key and important feature that was required.
And then finally, the ability in terms of functionality, the ability to know that the person wearing the device is indeed the person that is being assessed, and that there is that security built into the solution. Connectivity, no physical wires, the ability to support Bluetooth for users who may be hearing impaired that have a hearing impairment that would prefer to have a headphone capability with earbuds without wires. Again, to be able to hear and communicate with the person remotely.

And then last but not least, the solution, having the ability to actually capture digital artifacts for record retention, as well as other features that are considered part of the assisted reality, and augmented reality, and performance support capabilities in the device. We're thinking about future uses and applications within a clinical environment. For instance, from an audit perspective, but also from the ability to provide users wearing that device with support tools or, potentially, standard operating procedures on the device itself. So those were basically the main considerations that led Red Cross to the solution that we're sharing with you today. Thank you.

MS. MICHELE KLAWITTER: Thank you, Richard. So the considerations that Richard just shared with us were vetted within our most recent training modernization project, where we've introduced both AR and VR technology into our training programs. The AR device that you see here is the Realwear Navigator. And this today is just now starting to be used on the job training programs in our distribution and manufacturing locations. During the project, when we were doing our testing, we also saw an opportunity to explore the use of these devices to complete assessments.

So within our project, when we were doing our user experience trials for our training program, we also took the opportunity to do a small scale mock ACA test. So we began with having 32 impressions with two different devices, as Richard mentioned. This device, again, the Realwear Navigator, here proved to be the best suited for our specific requirements. During the test, we were able to confirm that all participants were able to complete the mock ACA, satisfying the requirements for direct observation. We didn't identify any tests within our trial that would not successfully be performed through this virtual method. We concluded that it took the same amount of time for the completion of the ACA virtually as it would in person, but it would eliminate the need for travel, and would add flexibility for scheduling and for our workforce planning by not pulling staff from other lab tasks to complete assessments within that same space. We also confirmed that the first person viewpoint was a significant benefit. Staff who responded to our surveys at the end of the trial shared comments like, the virtual ACA method was just as easy or even easier than in person. The first person viewpoint gave a better view than some in-person scenarios, and then our staff who were being assessed also shared that they felt like they were working comfortably alone, and they didn't feel like someone was watching them.

So overall, we asked the participants to rate the efficacy of the virtual ACA. 100% of the participants said the virtual ACA method was as easy or easier than the in-person method, and 90% of participants said the virtual ACA was as effective or more effective than the current in-person model. The 10% who didn't find it as effective actually were using the other device as part of our trial. And so that feedback helped guide our decision to choose the Realwear Navigator as our device. On the next slide, I'd like to walk you through the overview of the mock virtual ACA experience that we tested, just

to give you an idea of how this might work. So first, the staff member who is being assessed receives the device, and they fit it to their needs. This includes determining their dominant eye and fitting the device to the comfort level of their head. The virtual assessor initiates the connection to the assessee. So while the assessor is sitting at their laptop or a tablet, they initiate the session with the system, and the system sends a secure pin to the staff member who would be assessed via email.

So this is how we establish that secure and unique Connection within our single sign-on framework. They then complete the direct observation portion of the assessment with open communication throughout. Because some of the assessments may take a few hours to complete, the device can run continuously with hot swappable batteries that are provided with the device to maintain that connection to the session throughout. And then finally, the assessor would document completion. So on the next slide, I'll share what we defined as the assessor responsibilities during the virtual assessment. But first, just to note, the assessor would be expected to meet the same training requirements as our assessors do today with the addition of completing a web-based training on how to use the AR device-- any troubleshooting to-- standard troubleshooting with the person being assessed, and then how to capture documentation as needed. So as you see here, what we defined as assessor responsibilities during the assessment would include inviting the assessee to join the session, completing the direct observations requirements as appropriate, asking any interview questions that may be associated with that ACA checklist, and then capturing the documentation as necessary.

I'd like to now visit, on the next slide, some feedback, and revisiting the feedback that I shared with you just a minute ago, and really key in on one of the significant advantages that this wearable device can bring. So these images are taken directly from the video that Michelle shared earlier as we started our time together today. And really, this device allows for such an impressive first-person vantage point versus over-the-shoulder or shoulder-to-shoulder view.
So because it's completely hands-free and worn on the head, wherever the staff looks when they're turning their heads, that's what the assessor sees. It's not like the other fixed devices, as Richard was explaining, that you have on a phone or your computer laptop. Also the microphone and speaker allow for that easy communication between the pair. So for example, the assessor can ask the staff to zoom in or out to be able to see more closely to a particular form that they may be documenting.

They can also turn on that flashlight for better visibility and other actions. So overall, this was considered to be less intrusive for all parties involved and actually more like the regular workday in the lab environment for both the staff being assessed and other staff working in that lab as well. Michelle, I'll turn it back to you.

MS. MICHELE KLAWITTER: Great. So before we jump into some common questions and concerns, I'll just say that with any change to a process, and in particular, this level of change that we made in our training system, and especially when you're introducing new technology, you have to identify the potential risk and mitigate those in advance. And Red Cross quality assurance was a key stakeholder and final approver in all the design and development of our new training program.

And we were really focused on ensuring that key control points and the same level of rigor remained in place with our program as we had previously. Obviously, we did not want to take any steps back in our ability to provide quality outcomes. And so together with quality, together with our execution and process partners, monitored key quality indicators and our business and quality objectives after the implementation of our training program, and really looked at problems and non-conformance data post-implementation to look for any adverse impact.

We would employ that same level of scrutiny should this technology be approved for use in our laboratory competency assessment program. But to get back to some of the common questions and concerns, obviously, when you're using this technology, it's great. But it also introduces additional things you have to take into consideration, like what happens if you have poor connectivity? Well, I think we all know that connectivity is important, that that has to be something that you test during your trials and your pilots within your solution and in use in your facilities, which we did.

We also know that allowing enough time in advance so that not doing your assessments last minute, where you're now up against a due date, allowing some time should you run into any issues or unexpected situations. And obviously, you may need time the day of to troubleshoot some of the technology. But we want to also state that we recognize that this program would always have the fallback option of completing an in-person assessment. And we would build that into our program to have that as a secondary option. So the next one, how do you confirm the identity? We have talked a little bit about the PIN. I did want to just point out that PIN is delivered to the person being assessed through the use of our single sign-on email network. So they have to be able to get in and get the PIN. And that PIN is also-- it is specific to that session. It is session unique so that it couldn't be used for future assessments, et cetera. It's only limited to that session.

So what about the visibility for the assessor? You do need good bandwidth requirements to ensure that continuous connection and streaming capacity. But it's great that the camera for the assessor can zoom in and zoom out. And I hope that all of you saw in that side-by-side picture that Andrea just showed-- I mean, the assessor is now able to even see

down to the level of agglutination or whatever the test may be. They can look at the-- just have a much better viewpoint than we're able to get now over-the-shoulder. And so then as far as documenting steps, how can this assist in documenting the steps and tasks being observed? The capability within the system is such that you can do video captures and screenshots of what the assessor is seeing that would then allow for those to be used as documentation. I think that there's a lot of potential in that-- that that could be added to our records for retention. I will just acknowledge that when we're talking about digital record storage, you always have to take into consideration storage space. And so Andrea mentioned that some of these assessments can take multiple hours. I don't know that the right goal would be to capture multiple hours of video and try to store that somewhere. But I think that there are opportunities for critical control points or certain aspects that you're trying to identify and document. And obviously, then you would have to adhere to record retention guidelines also.

And then lastly, I think this is probably the one that causes the most pause for those of us in this industry is how does a virtual assessment account for the day-to-day disruptions that staff face? We're trying to ensure that we're assessing them in their normal working environment. Well, we actually maintain that the assessee is still in their normal working environment. They're immersed in their typical busy lab experience that they have day-to-day. But not having that assessor over their shoulder really actually makes it a more typical experience for the person being assessed. And we also think that the assessor can be in a more focused setting without disruptions. And I think that you all can envision that this technology can be used down the hall in a conference room in the same building or from 200 miles away. And we think that by having that flexibility, it really allows for just that flexibility in how we accomplish these assessments and how we can utilize those to utilize that to run our businesses better while still maintaining and ensuring that our staff have the same level of competency and skills in the work that they do. So with that, I'll just conclude.

We would like to thank you for having us here. We do contend that there's a place for the use of this technology and the important work that we do to confirm staff's competency to do their jobs and do it well. We've seen enormous benefit in other parts of our training program, and we really think that could apply to these types of assessments. For assessments, as Andrea mentioned, we did a short pilot or user experience. We would love to be able to do this at a broader scale because we do think that there are other benefits that have not yet been able to be even realized or fully known that we would like to further explore. We talked about flexibility and scheduling these assessments, not having to pull other staff offline to be the assessor, the ability to handle these assessments during staffing shortages. We're all faced with staffing shortages in our laboratories. And I think that we all know during unknown or unforeseen situations, like the public health emergency we saw during COVID, this was a great alternative. And to have this integrated into our systems and then be able to utilize it when we need to would really position us well for the future. I do think that we could wind up seeing maybe fewer assessors who are specialized in the specific test or laboratories that they're assessing. And by having that specialization with assessors, are we then providing more consistency in the evaluations of these staff's skills and abilities? Does that then drive further standardization in how our laboratory staff are being trained and evaluated, which is something that we're always looking into improve as an organization who is spread geographically across the country. And then also just the ability to document the electronic and the digital screen grabs that we could get from this type of technology during our assessments is just really attractive to us, especially myself in quality. So really, in conclusion, we believe that this wearable technology, when it's integrated into a well-designed competency assessment program, is equivalent or could even improve the assessment process that we have in place today. But with that being said, it is the technology together with-- hand-in-hand with a program that would have to be defined. And obviously, we all have the same common goal that we end up with well-trained, competent staff to ensure patient and recipient safety. And so knowing the enormous potential here with this type of technology, and that this really is, I feel, a turning point for our industry, I do think that-- I do want to offer that Red Cross is eager to partner with CMS to lead the way or to help share our experiences and the technology that we're using. And so, again, I just thank you all for having us here today. And let me just check my time. With that, I think we will conclude. And I will ask Andrea and Richard to join me in opening up for any questions. So thank you.

CLIAC CHAIR: Thank you. Yeah, any quick questions from the committee? [CLIAC MEMBER], I see your hand up.

CLIAC MEMBER: Yes, that was great. We previously saw some headset education for training people on how to use equipment at our last CLIA meeting, which was great. My question is, what does a headset like this cost? I mean, there must be savings with the competency training, and assessment, and all that. But one of the limitations has been the cost of these kinds of headsets. So I'm just curious.

CLIAC CHAIR: And before anyone answers that, Michelle, I just want to make sure you're still sharing your screen

MS. MICHELE KLAWITTER: Am I? Let me stop sharing. Maybe that's why I can't [AUDIO OUT], yeah. Thank you. I'm like, too many things. We're a Teams company, so Zoom is a little bit new to us. So thank you for your patience. I will let either Andrea or Richard chime in on that. I will say, first of all, just to be clear, we are not using this in our competency program today. I think Greg's probably happy to hear that. But we'd love to because we do think that there's a financial benefit as well as a quality benefit from doing it. But--

CLIAC MEMBER: No, I think it's great. I'm just wondering what the actual cost is of a headset.

MS. MICHELE KLAWITTER: Yeah, we are using it in other parts of our organization. So Andrea or Richard?

MS. ANDREA NOON: Go ahead, Richard.

MR. RICHARD REDMOND: So the cost to a business consumer is anywhere between $2,200 to $2,800 depending on the device that you use and the requirements that you have. But generally in that range. And then, of course, there's the software on the platform side of it, which is somewhere in the range of $60 to $100 per device, depending again on the licensing model that-- and there are a number of them out there in the marketplace that offer different collaboration software solutions as well. But you would expect to be somewhere in that range on both fronts.

MS. ANDREA NOON: For our programs, I would add to is we were considering the various models for how we have these devices allocated-- is for some of our larger facilities, would look at having these available and more consistently stored at those locations. And having more of a shipment model for our smaller staff where we don't have-- or smaller locations where we don't have as many staff.

CLIAC CHAIR: Thank you. [CLIAC MEMBER]?

CLIAC MEMBER: Yes, three separate questions. And the first one pivots off the statement "our locations." As you have done the due diligence on this approach, what's in my mind is that the technology and workflow will be applied to facilities that know that you've actually-- that your inspectors are already familiar with that you can actually even do due diligence on the physical workspace that these assessments will be in, which means you have that fourth variable also taken care of, which is the site and the actual laboratory. Have you thought through-- I could call it risk, but I think it's a broader question of reliability for locations that you're not familiar with. Because for the broader use of this technology and remote assessors, they would potentially have no idea what this facility was and what the potential risks are for an adequate assessment of competency. That's one question out of three. The other two are much shorter.

MS. MICHELE KLAWITTER: Yeah, Andrea, do you want to take that?

AMS. ANDREA NOON: What I would say-- as we began to evaluate what this program might look like, because as Michelle mentioned, we're not actively doing this today-- to factor in some of that, we do also want to acknowledge that this would require our local supervisors to have engagement as well. So there are some things that the supervisor would help with from the scheduling perspective and any additional support that might be necessary. So we would also look to that local team to help potentially identify any of those risks that an assessor who may not be familiar with that particular site should be looking for.

CLIAC MEMBER: And I could see a checklist for, in essence, the facility to host this technology more broadly applied. Second of three questions-- I seem to remember the video mentioning voice recognition, but I didn't hear further comment about that. And it occurs to me that once the initial chain of custody for subject identity is established, is voice recognition basically the follow-through to make sure that there's not a hot-swap of the device? In other words, if the voice recognition establishes the signature of the person being assessed, and then that would remain their signature through the duration of their assessment, particularly if there had to be a break for whatever reason.

MS. MICHELE KLAWITTER: Richard, do you want to speak to that?

MR. RICHARD REDMOND: It's definitely an interesting thought. And certainly with artificial intelligence solutions that are out there, that's actually being explored today, but slightly different context than here. The device with respect to using voice recognition is the ability for the end user to operate the device. Simple controls, like being able to zoom in, or change the quality setting in terms of the quality of the camera feed, and so on and so forth, or to terminate the call. They use their voice instead of physically interacting with the device itself. However, that doesn't necessarily rule out the ability to use a biometric method, like voice recognition, to confirm the identity of the end user. But it certainly isn't something that we have explored specifically with this particular hardware and software solution to this point, but it is possible.

CLIAC MEMBER: Not profound, but I've just given you an idea. Third is very simple. The visuals that you provide are people who are well-coughed with hair. And I'm just wondering if head and scalp comfort are something that are considered for the design? I could picture a strap over the top or something like that. I think about the sustained, in essence, compression on your scalp as you're going through this, and that might be a dissatisfier. No need to answer, but I could see issue with that.

MS. MICHELE KLAWITTER: Yeah, lots of considerations.

CLIAC MEMBER: Thank you.

CLIAC CHAIR: Guys, thank you. I see there's a lot of questions. I want to make sure we-- because we're not fully entering the discussion mode. These are to make sure that the hands that are up now are questions for the speakers, because we do have to get to the public comments as well. So [CLIAC MEMBER] and [CLIAC MEMBER], are these questions targeted for the speakers?

CLIAC MEMBER: Yes.

CLIAC CHAIR: Let's just try and keep them brief so that we can get to the public comments because we have those folks waiting. Go ahead, [CLIAC MEMBER].

CLIAC MEMBER: I don't know if you mentioned this before. And if you did, my apologies, but when you're using this device, is it recording? Is it recordable?

MS. ANDREA NOON: It can. Yes.

MS. MICHELE KLAWITTER: Yeah, so the assessor is on a laptop that-- and I won't get into too much of the technical. Richard would have to do that. But there's a program, and they can see. And then you're able, just like you could on your own desktop, to record, take screen grabs. And just like-- I said a lot. It has to be part of a developed program. Because then we would have to say, well, what do we want to grab-- at what point? Where do we want to store that digital record? And that would have to be built into the checklist that we have for the assessors.

CLIAC MEMBER: That makes sense. Thank you.

MS. MICHELE KLAWITTER: Sure. Thank you.

CLIAC CHAIR: [CLIAC MEMBER]?

CLIAC MEMBER: Thank you. My question goes to our earlier presentation this morning on cybersecurity, because you're looking at patient information through those devices. You're storing the information. And there's a risk there that that information may be a cyber risk. Could you address that?

MR. RICHARD REDMOND: From a technology standpoint, the connection between the remote person who's viewing remotely and the person wearing the device is encrypted to the highest standards possible. And one of the reasons that we look at the recording of digital information and the storage of that is really important factor, particularly for PII information that is being captured and transmitted. So we do explore those considerations from a technology/technical standpoint in terms of the streaming of the content that's being recorded by the camera, but also by the person speaking-- that that is encrypted between both endpoints-- the device itself that the assessee is wearing and the device that the remote assessor is accessing that information on.

CLIAC CHAIR: Excellent. [CLIAC MEMBER]?

CLIAC MEMBER: I think mine's connected somewhat to the same vein. When we're talking about positive identification of the person being assessed, you said it's tied to single sign-on. It's by email. How does it reset? Is it automatic when the headset's removed so that it would reset and have to be re-authenticated? I guess that's my first part of my question. The second part of my question-- is it exclusively tied to email? Or is there an opportunity for that to be something like through Duo so there-- you could access maybe similar modes of authentication that might already exist in your facility? I think that's the end of my question.

MR. RICHARD REDMOND: So I'll take the I'll take the first part of that. And the answer with respect to the PIN-- the person that initiates the PIN is the assessor. So they have to type in the assessee's name and email address. The system sends an email to the assessee who can only access that email, obviously, by logging in to their Red Cross email account on their computer or device to retrieve that PIN. When they connect to the session with the assessor using the device and the PIN, at that point, they are connected. Now, when the assessor terminates-- ends the session, that PIN is no longer valid for anyone. So in order to re-establish, the assessor would have to re-establish connection with this individual. The assessee would have to follow the process to have the PIN emailed-- a new PIN emailed that the system generates randomly. And it's 6-digits, and it's emailed to the person. Now, there are other forms in which that PIN can be provided and other two-factor authentication methods that can be used as well. So for instance, instead of the PIN necessarily being sent via an email message, it could be sent through SMS. In fact, that capability exists today. There are also other

methodologies that can be explored as well. So for instance, the device itself generating a random PIN, which is then shared with the assessor who then logs in and opens the session that way. So there definitely are different methods to providing that security and to having second factor security in addition to the second factor security that already exists within the Red Cross single sign-on methodology.

CLIAC MEMBER: Thank you.

CLIAC CHAIR: Yeah, I always look for simple solutions. And I hear the concern about the wrong person getting assessed. But handheld mirror could also do very similar functions-- just pointing at the camera and confirming this. [CHUCKLING]

MS. MICHELE KLAWITTER: Sure.

Public Comments

CLIAC CHAIR: Let's go to public comments. [CLIAC DFO], we have one or two.

CLIAC DFO: We have two public comments. The first will be, again, from Dr. Diana Cardona from the College of American Pathologists. She will be followed by Miss Carlyn Mathews from the American Association for laboratory accreditation, or A2LA. So, Diana?

DR. DIANA CARDONA: Thank you. Good afternoon again. So again, my name is Dr. Cardona. I'm a practicing pathologist and the associate medical director at Duke Health. Here representing the College of American Pathologists. As I previously expressed, the CAP fosters and advances excellence in the practice of pathology and laboratory medicine by leading in laboratory accreditation and proficiency testing programs. The CAP supports CLIAs interest in reducing the burden of competency assessment, especially now as the CAP's accreditation checklist is actually under review by CMS. Competency assessment is a critical piece of ensuring laboratory quality, requiring pathologists in the role as laboratory directors to manage and track the qualifications, continuing education, and assessments for the laboratory staff they oversee. In the case of large laboratories, or when one individual serves as laboratory director for multiple laboratories, satisfying the current competency assessment requirements can take up a significant portion of their time, taking their attention away from providing patient care and diagnosis. CAP accreditation has not detected quality issues originating from the current CLIA competency assessment requirements, and as such, the CAP supports the current scope of competency assessment under CLIA and believes that expansion could have negative consequences in terms of staff burden and burnout without an upside of quality improvement.

The six required elements of competency assessment for non-wave testing include direct observation of routine patient test performance, which would include patient identification and specimen collection, processing, and testing. Monitoring the recording and reporting of test results. Review of intermediate steps such as worksheets, quality control records, proficiency testing results, and preventative maintenance records. Direct observation of instrument maintenance and function checks. Assessment of test performance through blind samples or external proficiency testing samples, and evaluation of staff member's problem solving skills. All but two elements-- those requiring direct observation-- can already be done remotely. However, direct observation can also be done remotely, as was demonstrated during the public health emergency, which proved that remote assessments can be practical and adequate. The requirements outlined in CMS's remote survey process during the public health emergency could inform the development of a permanent policy for remote competency assessment. From a technical perspective, conducting direct observation remotely is entirely feasible.

The CAP and other accreditors conducted some inspections remotely using off-the-shelf technology. The CAP found that conducting remote assessments via video calls on a mobile device-- for example, a laptop on a wheeled cart or a smartphone mounted on a tripod-- provided enough sight of the laboratory work being done to satisfactorily assess competency. Enabling assessments to be done remotely without a supervisor traveling and without laboratory personnel modifying their workday or workflow to accommodate an additional person in a laboratory will save time and resources while still maintaining a high quality standard. Small rural hospitals or clinics where a single technologist is working may benefit the most from this possible option. To maximize the benefits of moving to remote observation, the technology involved must be readily available, affordable, and easy to implement. Requirements for remote observation of competency assessment should be developed using a consensus-based approach to gain a solid understanding of CLIA's goals and the capabilities and challenges specific to current laboratory practice. One of the challenges might be ensuring that competency records are maintained and available at the location with that CLIA number so that all records are available for inspections. Additionally, to identify suitable technological tools for conducting remote assessment, CMS should clarify what view is needed on the screen. For example, does it need to be from a first-person vantage point? And when competency assessment is done using real patient samples, considerations would need to be made around how protected health information is viewed and stored. Once again, thank you for your time today. And as always, we welcome the opportunity for further dialogue.

CLIAC CHAIR: Thank you. We have another one.

MS. CARLYN MATHEWS: Hi, my name is Carlyn Matthews, and I am a clinical program manager at A2LA. A2LA appreciates the opportunity to provide comments to CLIAC for your consideration. A2LA has been offering accreditation services for over 45 years. We currently hold CMS team status as well as international laboratory accreditation cooperation recognition to provide clinical laboratory accreditation. A2LA is the only accreditation organization in the world to achieve and maintain both these formal recognitions. Over the years, A2LA has performed thousands of remote assessments in different capabilities and has gained valuable knowledge on the remote assessment process. We wish to highlight some points for your consideration that may make virtual assessments more widely accepted. A primary objective when performing a virtual assessment is that the assessment is held to the same level of rigor as an in-person assessment. A2LA uses resources provided by ILAC in order to help us meet this objective. A2LA only considers if an assessment activity is a candidate following an assessment by first ensuring that the laboratory is eligible for remote assessment by following the remote assessment policy, which includes conducting a risk assessment. A risk assessment is an important tool that should be used in the laboratories, policies and procedures for virtual competency assessments. A risk assessment is the overall process of risk identification, risk analysis, and evaluation of risk. According to ISO 13-- or 31073 and is initiated early in the planning stages. The concept of a risk assessment should be applied to competency assessments in order to determine if a virtual competency assessment is viable. For example, for an accreditation organization, conducting a survey, A2LA considers these factors in a risk assessment. Previous survey technique, remote or in-person, number and nature of previous findings, depth of previous survey observations, laboratory scope, and laboratory resource change from the previous survey. Likewise, the risk assessment factors for competency assessments may include techniques for previous competency assessments, environmental conditions, outcomes and findings from previous competency assessments, external survey results for the area, and severity of findings, proficiency testing results, and staff turnover. Another factor that needs to be considered is if there is areas of the laboratory in which the testing would not be able to be easily observed due to internet connectivity issues or lack of visibility of the testing personnel, facilities, and/or instruments. An additional factor 1 needs to consider is the medium in which laboratory records are maintained electronically or paper-based and how readily available they are for review. This may lead to a higher risk that the competency assessment are not being held to the same standard as an in-person assessment. With a higher risk identified, the laboratories may decide that an in-person competency assessment is a better option than a virtual competency assessment. Ultimately, if the laboratory considers this to be a lower risk, the laboratory will need to develop a mechanism to share necessary records prior to the competency assessment occurring. This may significantly increase the amount of preparation and overall time in which the competency assessment occurs. A2LA encourages the committee to consider these topics as CLIAC continues to evaluate the use of virtual competency assessments. Thank you for allowing A2LA the opportunity to provide comments on this matter and considering us as a resource if any additional information is required.

Committee Discussion

CLIAC CHAIR: Great. Thank you. So we'll go through the-- we'll have our discussion now. I just want to make sure-- give me a second. I'll check out the timing. So yeah, we'll be able to discuss and come up with our recommendation between now and 4:55 PM Eastern time, which gives us quite a bit of time. So to frame the conversation, I would recommend that we actually go through these questions and have a discussion. I think the discussion will be very helpful, as especially be recorded and documented in minutes. But at the end, the output here will-- what we're really being asked for is either a recommendation in support of remote assessment or a recommendation against remote assessments to be included. So just to give a little insight as to what I'll be driving us towards. So let's just start off with the first question-- see if anyone has any comments or other questions-- is, what is the risk of losing direct in-person observation? You can see the sub-question-- background noise, odors, and other activities. What are the risks that the group sees with the remote assessment? Silence is deafening.

CLIAC MEMBER: Very little.

CLIAC CHAIR: Cool.

CLIAC MEMBER: Highly supportive of these ideas.

CLIAC MEMBER: Yes.

CLIAC CHAIR: Cool. Yeah, and just to reflect back to some of the things that were brought up already-- some nefarious swapping of the device so that you're actually assessing the wrong person. That would be a risk. Another risk that was also already called out would be PHI. It'll be transmitted, stored somewhere. So that was another risk. Any other? [CLIAC MEMBER]?

CLIAC MEMBER: This meeting alone attests to the fact that over the last four years, our society has become entirely comfortable with establishing an interpersonal relationship through a video mechanism. And I think we should not only acknowledge that fact, but embrace it as part of it.

CLIAC CHAIR: Yeah. [CLIAC MEMBER]?

CLIAC MEMBER: I was just going to mention the same thing. I am resoundingly in favor of moving forward. And I think that the areas that are mentioned as areas of risk are addressed in other areas of regulation and looking at the environment and environmental care, things like that. They're addressed in other areas that may-- it's not really-- I don't think competency is where we need to address things like environment, and odors, and things like that.

CLIAC CHAIR: Yeah, it was interesting. I interpreted the odor comment-- and I'm just sharing this in case I was wrong-- was actually part of the analytical process, particularly micro. Obviously, you wouldn't be able to touch upon that, but I don't know how often we actually rely on odor as part of our diagnostic process anymore. But back in the day--

CLIAC MEMBER: We should not be doing that.

CLIAC CHAIR: I would probably--

CLIAC MEMBER: If they're doing that, then we should cede that.

CLIAC MEMBER: Sorry, [CLIAC MEMBER]. We still do that.
[CHUCKLING]

CLIAC MEMBER: [CLIAC DFO], if I may, there's one place where odor plays a role, and that's in hazards. In other words, biohazards, and whether it's xylene or something like that. In other words, if you really have an evolving disaster, odor is definitely one of the cues.

CLIAC CHAIR: Yeah. [CLIAC MEMBER]?

CLIAC MEMBER: I think that this should be successfully embraced because we have a real workforce shortage of people who can do quality management. And this will make those folks a lot more productive and we can get more things done.
CLIAC CHAIR: Great. It feels like rolling a rock down hill. Heather, yeah, when you're done typing, if you go back up to the questions, we'll continue to go through them. What are the recommended limits of virtual competencies in terms of-- can you foresee any particular subspecialty within the laboratory being more challenging or less challenging?
Any type of instrumentation that may be impossible to assess remotely? Let's start there, and then we'll go through the other questions. So again, I find the silence to be really meaningful here. I also could not come up with any particular section of the laboratory where this couldn't necessarily be used. [CLIAC MEMBER]?

CLIAC MEMBER: I think the only thing that really comes to my mind is microscopy, and that's just based on this particular solution. Microscopy can certainly be assessed using adjunct technologies where you can follow what people are actually looking at on the microscope. In fact, eye movement and eye movement detection with microscopy is something that's being used very extensively for a whole variety of reasons, especially documenting AI, et cetera. But for this particular application, that's maybe a little bit of a gap, but I don't think that that's an insurmountable one. That's really the only one that jumps to my mind.

CLIAC CHAIR: Yeah. [CLIAC MEMBER]?

CLIAC MEMBER: I think the only thing that I would be concerned about is the variation. This particular technology that was presented was great because it was hands-free with that direct first-person look. And some of the other technologies aren't as user friendly. But overall, when I presented this to my techs as a possibility, just for learning new instrumentation, they were very excited about that change. So I think it would be very well-received with the younger techs in training.

CLIAC CHAIR: Yeah, it's a good point. And as we move forward-- it sounds like getting ahead of us, but it's not that the recommendation is going to be favorable. And so we can also help refine what characteristics the system should have-- or maybe let's do it-- we could do it in degrees of severity-- must-haves or are nice-to-haves. So as we come up with those ideas-- like first-person view, I think-- is it a nice-to-have, is it a must-have? I don't know. But certainly I think security and protection of PHI is a must-have. [CLIAC MEMBER]?

CLIAC MEMBER: Yeah, thanks for the opportunity to weigh in on this. And by this comment, it's a niche, and I think it's very public-health-focused. Doesn't mean that I'm not supporting this because I do agree with others about moving

forward with it. But one area where I don't think this would work is looking at-- I'm just going to use the term "select agents," which is something that-- in BSL3 work. So something that public health labs are very, very much involved in. You're in full PPE. That's not going to work. So as long as there are obviously exceptions to the rule where direct observation in-person, obviously, can substitute for that, then I think it's fine. But there are going to be exceptions to the general rule. I just wanted to make sure that was clear. Thanks.

CLIAC CHAIR: Yeah, good point and an important point, because this would be a tool that is allowed-- that laboratories could use. They don't have to use it. We could discuss offline. I'm just super curious. Direct observation in a BSL4 lab or BSL3 has to be pretty challenging to begin with. But yeah, a topic for another day. Workload limits of the number of people that could be assessed? How does everyone feel? To be honest with you, I think this is a reasonable question whether you're doing it remotely or not. Any particularly strong thoughts? Is it a concern of doing too many assessments in one day?

CLIAC MEMBER: Are you saying in one day or at one time, just to clarify? Is that meaning it should be one-- sorry, I talked out-of-turn, but are you saying it should be one-on-one, or you can't do more than one person at a time? Is that what we're saying.

CLIAC CHAIR: Very good point. So I interpreted that as number of assessments in a time period. So in a shift or in a day. It doesn't sound like the group has any strong feelings there. But in terms of concurrent assessments, this technology could probably at least enable that. And what is our comfort level with concurrent assessments? Like I, as the assessor, could assess three people at a time. That makes me a little more uncomfortable. Is that what your questioning was, [CLIAC MEMBER]?

CLIAC MEMBER: Yes. Not to speak out-of-turn, but yes.

CLIAC CHAIR: That's OK. It was-- but-- how does anyone feel about concurrent assessments? Is that a limitation we would recommend?

CLIAC MEMBER: Yes.

CLIAC MEMBER: Yes.

CLIAC MEMBER: Yes.

CLIAC CHAIR: Excellent. [CLIAC MEMBER], I see your hand up as well?

CLIAC MEMBER: Well, yeah, I was going to just agree with that point, that we limit this at least a little bit. It'd probably be best to use this technology for a while-- at least for the next couple of years-- one-on-one.

CLIAC CHAIR: Thank you. [CLIAC MEMBER], your hands up. It's funny, though. Your background perfectly hides the hand. Go ahead, Chip. I think you're muted. Fell off. Should we create on-site regulatory requirements for technical supervisors and technical consultants? I'm not quite sure I understand the question. I don't know if, [CMS EX OFFICIO], you have any background to the—

CMS EX OFFICIO: Yeah, so the only real regulatory link requiring that in-person presence under the regulation is this direct observation. So is this something that really isn't necessary-- the technical consultants and supervisors are going to be on site regularly-- or is this something that we have to actively require?

CLIAC CHAIR: But the scope of that question is-- and I guess it's kind of definitional here. The scope of that question is, do we need to create on site requirements for the competency assessment, leaving aside on site requirements for technical supervisors and consultants more broadly out of scope? Correct?

CMS EX OFFICIO: Yes, definitely.

CLIAC CHAIR: So, yeah, I guess the cognitive dissonance I'm having-- that if we're allowing remote assessment, by definition, we don't have on-site requirements for competency assessment. Am I missing something?

CMS EX OFFICIO: No, I mean, that-- yeah, just what should the extent of on-site presence of a consultant and technical supervisor be? And we can also pivot the question, because Heather, I think you mentioned this. You had recommended that first one be in-person just to familiarize yourself with the laboratory and the environment, and subsequent ones can be virtual. The difficulty with that is either a flexibility exists or it doesn't under the regulations. So without going through

rule change, we wouldn't be able to say that in just guidance-- that, well, the first one has to be in-person. So it's really a question of how rigorous do we need to be with on-site presence?

CLIAC CHAIR: Gotcha. Yeah, and that actually brings up a question I have, because it was hinted at a couple of times so far. My understanding is the only people who can perform the competency assessment are the supervisors, is the management team who-- they, themselves, are competent in the testing process. So for me, it was implied that the only people who would be doing this remote assessment would still be the site supervisors, which would solve all of the familiarity issues-- familiarity with the environment, familiarity with this SOP, even familiarity with the person who's being the assessee. But this technology could open the door for, say, third-party assessors of competency who would not have the familiarity with the environment, the specific SOP, nor the individual. So is that a line we want to-- I don't even know if we have to draw it because I think that line's already drawn. Do we want to continue to support that line-- that remote competency assessment can only be performed by site supervisors and management? [CLIAC MEMBER]?

CLIAC MEMBER: I guess my--

CLIAC CHAIR: I don't know if you have to have that correlated to that or something.

CLIAC MEMBER: No, my hands were up related to that. I guess my feeling is that I would not want to remove a level of familiarity with the technical supervisor or technical consultant with the location. I think there's a difference in being on-site for-- let's say you have five or six different team members that are available at that site. And you have to perform competency, and you have 100 different sites that you have to travel around. It's one thing to be familiar with all the different test systems, and making a visit, and making sure all the materials available there, that the temperature is where it needs to be, the records are being maintained, and helping support that, and being physically available to that, and then being able to remotely support competency versus never having been on site. And I think that that's a different level of support and familiarity. And I don't know that I think that you're able to perform an adequate competency if you're not at least making a physical visit.

CLIAC CHAIR: So what I'm hearing is obviously still keeping it with on-site supervisor management team. The nuance you added there is if your supervisor role or responsibilities are really multiple sites. But I would still imagine and expect there'd be a significant amount of familiarity with all of those sites that you're the supervisor of, right? That was kind of a question that I had, yeah.

CLIAC MEMBER: Oh, yeah. I mean, that's just my two cents.

CLIAC CHAIR: OK. [CLIAC MEMBER]?

CLIAC MEMBER: You'll hear a different opinion from me. I've been listening to this whole discussion with an entirely different perspective, that this opens up horizons for inter-institutional and cross-technology competence that could be mapped out as to what the obligate verticals are along the lines of what Heather was saying. But also the fact that when new technologies are coming in, it can be these subspecialist assessors who can, in essence, get a workforce off the ground even when the supervisor is not up to speed. And particularly given the extreme stresses on supervisors, both to keep the benches going as well as to manage-- to fulfill their management functions, I think a technology like this can provide a valuable adjunct to broadening the scope of competence assessment provided it's mapped out properly. So the third of three points I'd make is, in the end, this devolves to the medical director. We've had this discussion before at CLIAC which is, in the end, the medical director carries responsibility for the performance of the workforce. And while I think what I've said is beyond the current discussion, I would-- I'd like there to be some horizons that are available, at least in the eyes of CLIAC, if not in the specific wording that is recommended today. I think we need to be open to a broader geography of competence assessment than just an obligate direct vertical by supervisor.

CLIAC CHAIR: Yeah, I think that's a good point. What I'd dropped into that draft recommendation was competency continues to be performed by site management staff. And really, the essence of that is familiarity of location, local SOPs, et cetera. Now, to your point, to future-proof this a little bit, and future-proof the guidance, and to see how this technology could enable outside of institution competency assessment from third parties or experts across the country or world-- the link that I would want to maintain, though, is even if there's an external assessor, that they have intimate familiarity with the location, local SOPs, et cetera. To your point, I think pathology competency assessment of interpreting a slide is much more easily outsourced in the future to a third-party assessment. But running a blood gas analyzer, those SOPs can change quite a bit from site-to-site. And that intimate familiarity with that SOP is what's critical.

CLIAC MEMBER: And I think CLIAC can express opinions in this area as how this could be mapped out. I prefer the term "forward compatibility" as opposed to "future proof." "Proof" is like you're putting up a-- it sounds like you're putting up a barrier. But I think we're both getting at the same thing.

CLIAC CHAIR: Absolutely. [CLIAC MEMBER]?

CLIAC MEMBER: Yeah, I agree with Jim completely. I think it actually would be an enhancement to our workforce if they were the competent person, say, in a molecular arena, and they were able to do the assessment for other technologists in that arena. I think it would increase job satisfaction, and it would lower the work burden on the supervisor. And I had many technologists that are teaching technologists. If they can teach the bench, why couldn't they do a competency assessment? So I think it's up to the laboratory director. And I think it should be much broader potentially.

CLIAC CHAIR: Cool. [CLIAC DFO], when you get a chance, if you could scroll back up. Last two questions. Should this be test-specific or, I guess, providing some flexibility? I think this is a perfect opportunity to-- at the discretion of the lab director-- what the lab director is comfortable with. Again, when challenging the group before about are there any segments or instruments that would not be amenable to this type of remote assessment, everyone was pretty quiet. But I guess we'll ask it again-- see if anything else comes up. Just for completion's sake, I think we're all highlighting some of the benefits. Are there any other benefits that we have not addressed so far? Those include workforce shortages, increasing bandwidth, more efficient, competency assessments, reducing travel time, et cetera, things like that?

CLIAC MEMBER: [CLIAC CHAIR], sorry. I didn't get off mute or raise my hand quick enough or get it down from the last one. But previously, the one thing that I would be hesitant about on the competency is if there was significant result interpretation that was needed and if that-- what level of competency somebody might have to do in that training.
So for instance, if you have a microbiology of an organism and a resistance determinant, can you tell a doctor what kind of drug they can use. Like that kind of thing. I think some of those things, where there's a lot of interpretation, would have to have a better level of competency training, where you might have to have the supervisor. So I think there are some exceptions, like we talked about with BSL4 potentially.

CLIAC CHAIR: Jim, is your hand back up or--

CLIAC MEMBER: It is back up. Yes. you're asking if there are other advantages. Again, I've been thinking all these things right from the very start, which is going back to the pipeline and the remarkable opportunities through OneLab virtual reality, for example, for training to the extent that a virtual OneLab then transmutes to, OK, dear student, walk into a lab-- and Heather, in this case, I would say who is familiar to the instructor. And so we moved from the virtual to the real. And the instructor can actually perform a proficiency and a competency assessment. And not unlike EPA's-- the professional assessments and graduate medical education for physicians, a student-- a trainee could accumulate a portfolio of assessed proficiencies through the course of their training prior to going into the laboratory. And in essence, creating a more democratized landscape for the competencies of our pipeline as they prepare for entering into the workspace so that a supervisor could take in a student either through the required in-lab experience or even for hire. And say, OK, we already have this portfolio of assessed proficiencies thanks to this democratized virtual-to-assisted reality environment. And I think that is another mechanism for enhancing our pipeline.

CLIAC MEMBER: Oh, Jim, are you suggesting competencies that aren't-- that transmute CLIA certificates?

CLIAC MEMBER: I'm probably well out of my lane by now, but--

CLIAC MEMBER: Oh, my goodness.

CLIAC MEMBER: But what I'm thinking of is the fact-- if we recall, OneLab in virtual reality, it's a rather small step to do in a physical lab assisted reality competency assessment. And bingo. The trainee now has-- builds their portfolio of-- use the word you want, [CLIAC DFO]-- established competencies.

CLIAC MEMBER: Hey, this is a revolution. Let's go.
[CHUCKLING]

CLIAC MEMBER: Again, this is a landscape which I think can democratize our pipeline. And I continue to look at the map of the United States and the appalling asymmetry of where training programs are to where need is.

CLIAC MEMBER: I'm in rural Eastern North Carolina. Tell me about it. [CHUCKLES] I love it.
CLIAC CHAIR: Excellent. All righty. So it sounds like there's a tremendous amount of alignment. Heather, I would just say one thing-- that as you're moving things around, that first person view, I don't think that's a must-have. I think the other three are. And maybe the refining of the second must-have-- the spirit there is that the competency assessor must have intimate familiarity with the local laboratory and procedure. So then it's a little more future compatibility in terms of who that person is. It doesn't necessarily need to be a supervisor, but they must have that familiarity. So we have a draft recommendation up ahead of us. Again, the goal was to leave here with a recommendation that we're either for or against remote assessment. I think our support of remote assessment is clear. So the recommendation is to allow remote

assessment to be utilized in the direct observation component of competency assessment. And then, obviously, we have a whole bunch of considerations for the agency as that guidance could be written. So let's take a second to just quickly look at it. If there's any modifications we want to make to it, let's do it. And then we can move forward with the motion. All righty, any modifications? Do we have a motion?

CLIAC MEMBER: So moved.

CLIAC MEMBER: I move.

CLIAC MEMBER: Second.

CLIAC CHAIR: OK, second. All those in favor, please raise your virtual hand. We have a majority, so the motion passes. Thank you very much. I don't believe we-- I think we've successfully completed this topic, so I think we can conclude that topic. [CLIAC DFO], I know we're ahead of schedule a little bit. In terms of other topics, do we want to have a free flowing-- potential future topics-- do you want to have free flowing conversation now or would you prefer to do it online?

CLIAC DFO: Yeah, sure. Since we have a few more minutes left, we did-- we typically have a little bit of time for future topic recommendations, but our agenda was packed. But if anybody has anything off the top of their head, we have 15 more minutes. And please, as a reminder, they must all relate to the CLIA regulations. But yes, I'm not going to type them on a sheet of paper. This is all being recorded. We'll have the information.

CLIAC CHAIR: Yeah, just take a few minutes. If anyone has any ideas of topics we want to discuss in future CLIAC meetings, feel free to share it. So I see [CLIAC MEMBER], [CLIAC MEMBER], [CLIAC MEMBER], and [CLIAC MEMBER] all have your hands up. I don't know if they're just remnants of the vote or not, but—[CLIAC MEMBER], go ahead.

CLIAC MEMBER: They're remnants.

CLIAC MEMBER: Yeah, it's from the vote.

CLIAC CHAIR: OK, it's from the vote. [CLIAC MEMBER], you're also from the vote?

CLIAC MEMBER: Yeah.

CLIAC CHAIR: [CLIAC MEMBER]?

CLIAC MEMBER: My hand is up.

CLIAC CHAIR: Go ahead.

CLIAC MEMBER: I think it was the CLIAC meeting where Million Hearts was discussed, where there was a CLIAC motion for a working group, in essence-- call it a population health working group. And I am hoping and waiting for that to come around on the CLIAC agenda-- is when that recommendation will be activated.

CLIAC CHAIR: Great. Thank you. Kim, I saw your hand up. I don't know if that was-- no? OK. All righty. Heather, do I have to do a motion to adjourn? Yeah? Well, before I do the motion to adjourn, I did want to just thank everyone for a really wonderful two days. We covered a lot of ground, came up with some really good and refined recommendations. So I think a wildly successful November CLIAC meeting. Just as a reminder, our next meeting will be in Atlanta, Georgia, on April 9th and 10th in 2025 at the--

CLIAC MEMBER: In-person?

CLIAC CHAIR: It will be in-person, yeah.

CLIAC MEMBER: Bravo.

CLIAC CHAIR: So there will be a Zoom option as well. But of course, we strongly encourage physical participation. We just like hanging out with all of you guys. And if you have any other potential topics to discuss, please feel free to email CLIAC at cliac@cdc.gov. So with that, do I have a motion to adjourn?

CLIAC MEMBER: So moved.

CLIAC CHAIR: Second. I'm going to dive this way. Do we have to vote on adjourning?

[CHUCKLING]

CLIAC MEMBER: All good.

CLIAC DFO: We're done. Thanks, everyone.

CLIAC MEMBER: Thank you, everyone.

CLIAC MEMBER: Thanks, Heather.

CLIAC MEMBER: Bye bye.

CLIAC MEMBER: Thank you.

CLIAC MEMBER: Thanks, everyone.

CLIAC MEMBER: Thank you, everyone.

CLIAC MEMBER: Good bye.

CLIAC CHAIR: Take care.

CLIAC MEMBER: Bye bye.

CLIAC MEMBER: See you.