The CLIAC Next Generation Sequencing (NGS) Workgroup Report

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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

- Nirali M. Patel, MD – Workgroup Chair
- Heather L. Stang, MS, MT – Workgroup DFO
- Diego Arambula, PhD – CDC Ex Officio
- Penny Keller, BS, MB(ASCP) – CMS Ex Officio
- Amy Zale, MT(ASCP) – FDA Ex Officio
- Tariq S. Adwan, PhD
- Heather M. Blankenship, PhD
- Chester W. Brown, MD, PhD
- Alexis B. Carter, MD
- Marsha Deitz, MBA, MLS (ASCP), CQA (ASQ)
- Birgit Funke, PhD, FACMG
- William A. Glover II, PhD, D(ABMM), MLS(ASCP)
- R. Tanner Hagelstrom, PhD
- Susan Hsiao, MD, PhD
- Eric Klee, PhD
- Ravindra Kolhe, MD, PhD, FCAP
- Christina Lockwood, PhD, DABCC, DABMGG
- Duncan MacCannell, PhD, MBT
- Steve Miller, MD, PhD
- Kimberlee A. Musser, PhD
- Honey Reddi, PhD, D(ABMGG), FACMG
- Jason N. Rosenbaum, MD
- Marie-Claire Rowlinson, PhD, D(ABMM)
- Cynthe L. Sims PhD, HCLD(ABB)
- Eric Weimer, PhD, D(ABMLI), F(ACHI)
- 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 for presentation during the next meeting.

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