

April 8 2019

APHL Public Comment

Clinical Laboratory Improvement Advisory Committee Meeting April 10-11 2019

The Association of Public Health Laboratories (APHL) appreciates the opportunity to comment on the Clinical Laboratory Improvement Advisory Committee (CLIAC) Next Generation Sequencing (NGS) Workgroup report.

NGS technology has been utilized for many different applications from infectious disease characterization to genetic disorders to cancer genomics. APHL member laboratories are moving to use this technology for infectious disease detection, characterization and surveillance, and newborn screening. Any guidelines, requirements or regulations must account for the diversity of genomes being sequenced and the variety of NGS applications.

The NGS Workgroup report reflects the unique challenges and considerations around NGS. The report focuses on challenges related to human genetics, including those that may be relevant to newborn screening, an important program for APHL member laboratories. While it includes references to the unique challenges inherent to NGS of microbial organisms, we would like to emphasize differences between microbial NGS and human NGS related to quality assurance, quality control, validation and data management approaches as there may be deleterious consequences for the work of public health laboratories if these differences are not accounted for.

Points we would like to highlight are delineated below:

- The workgroup recommended that “validation should be driven by the use case for the test in the clinical context.” We would like to emphasize the need for this as, unlike the testing for human genetic disorders and cancer, there are no commercially available or gold standard materials to use for validation for some microorganisms.
- There was a recommendation to use standardized and commercial PT programs. This would not be feasible for many infectious diseases as no commercial test is available. The workgroup did note the need for more “microbiology NGS PT.” This lack of commercial tests and widely available standards should be noted when making any guideline or regulation around PT.
- In reference to validation and PT, we appreciate the workgroup noting that “an all-inclusive guideline is challenging as there is a fear of being restrictive.” Our members would welcome guidance that is flexible enough to accommodate not only the differences in human versus microbial genetics, but that is also reflective of the diversity of microorganisms tested by APHL member laboratories.
- Within QA and QC, it was noted that some of the “metrics need to be organism specific and experience is needed to define the metrics.” We concur that beyond the delineation between human and microbial genetics, flexibility and allowances for differences within microorganisms is imperative. The workgroup posed the question of whether laboratories could utilize the Individualized Quality Control Plan (IQCP) to determine the proper amount of QC needed and our members also concur with this suggestion.

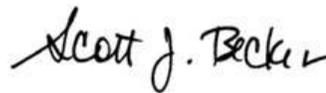
- The lack of CLIA guidance around bioinformatics was noted throughout the findings. This aligns with public health laboratories' experience in microbial genetics. The report noted that there needs to be "harmonization and curation of databases." These databases often determine the output of bioinformatics pipelines and the lack of harmonization of databases or specifying which databases are being utilized remains a challenge for microbial genomics.
- Data management is a substantial challenge that results from the amount of data generated by NGS. Data retention policies, including which files should be kept and for how long, should take into account the type of organism. Given the differences between genetic testing around human versus microbial samples, any guideline or regulation around data storage should take into account these differences.
- The report states that guidance is needed regarding "what files to store; raw data vs processed vs intermediate files". We would like to emphasize this point, also taking into account the policies and procedures for re-analysis of any raw data given the updates to the software and code and database changes that can occur.
- Bioinformaticians are a new segment of the laboratory workforce and as stated in the workgroup summary, there are no "personnel requirements for the bioinformaticians as the current CLIA personnel requirements do not fit clinical informaticians." If regulations are added regarding bioinformaticians, the definition of a bioinformatician should be examined, particularly as public health laboratory staff may review analytic outputs and interpret the data even if they are not responsible for the creation of the analytic pipelines.

Thank you for this opportunity to share our concerns and highlight the items of greatest consequence and relevance to our members on the use of NGS in microbial genetics.

Sincerely,



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APHL works to strengthen laboratory systems serving the public's health in the US and globally. APHL's member laboratories protect the public's health by monitoring and detecting infectious and foodborne diseases, environmental contaminants, terrorist agents, genetic disorders in newborns and other diverse health threats.