Statement from the
American Society for Clinical Pathology
to the
Clinical Laboratory Improvement Advisory Committee

The American Society for Clinical Pathology is pleased to provide this statement to the Clinical Laboratory Improvement Advisory Committee (CLIAC) on the roles, responsibilities and competencies of bioinformaticists. The completion of the Human Genome Project has resulted in vast sums of patient data, and bioinformaticists are increasingly being utilized by clinical laboratories to manage, process, and analyze it, especially in the rapidly expanding specialty of molecular diagnostics. Bioinformaticists, and the unique skills these individuals bring, are also helping to transform the practice of pathology and laboratory medicine by developing or/or enhancing the bioinformatics tools used to expand the ability of pathology and laboratory medicine to protect patient health. ASCP greatly appreciates CLIAC's leadership by focusing attention on the valuable contribution these professionals are making and to improve their ability to do so.

The following comments are based on comments provided by our membership during our efforts to respond to the questions posed by the CLIAC.

CLIAC Discussion Questions:

Question 1: Are Bioinformaticists needed in clinical and public health laboratories? If so, what are the current roles, responsibilities, and competencies of bioinformaticists in these settings?

ASCP believes that bioinformaticists are a key component of high quality, full service clinical laboratories, though the roles and responsibilities of these professionals may vary significantly.

Informaticists are critical to building the bioinformatics pipeline, which can include the software and database engineering, configuration of available bioinformatics software, and/or management and interfacing of LIS and other informatics systems, both internally within the laboratory (e.g. instrument interfaces) and externally (e.g. client or outreach interfaces). Today, clinical laboratory testing increasingly relies on algorithmic processing of one or multiple test results to derive different types of clinical indices, risk assessments, etc. While many of these are proprietary (vendor-specific), some are developed and managed internally by individual clinical laboratories--from tests like estimated

glomerular filtration rate and calculated LDL cholesterol levels to tests as complex as prenatal aneuploidy risk based on maternal biochemical profiles.

With respect to emerging technologies, much attention is being devoted to informatic management of next generation sequencing data for a number of applications (molecular oncology, carrier testing, syndromic testing, non-invasive prenatal testing (NIPT), etc.). It should also be mentioned that with specific respect to public health laboratories, more and more states are requiring electronic reporting of reportable diseases with specific requirements on the transmitting of demographic data, contact information, etc. As a result, all clinical laboratories, regardless of size, must effectively gather appropriate information and interface with state or county public health departments for effective reporting. These tasks are often handled by bioinformaticists.

ASCP is unaware of any comprehensive data that specifically addresses the training and competencies that should be required of bioinformaticists working in clinical laboratory settings. Some bioinformaticists have training in the laboratory sciences prior to transitioning into bioinformatics while others have training rooted in statistics and computer/data sciences prior to their work with clinical laboratory data. Though ASCP is a strong supporter of rigorous and appropriate academic and clinical training for pathologists, other physicians, and non-physician laboratory professionals, we believe more information is needed before a particular set of personnel standards should be articulated for these healthcare professionals. That said, we believe that CLIAC would be well served by seeking additional data on the key competencies that should be expected of these healthcare professionals. As a result, ASCP strongly encourages CLIAC to urge the completion of a bioinformatics workforce survey to of these health care professionals.

Question 2: What areas exist in CLIA where specific requirements or guidance might be needed to ensure the accuracy and reliability to new and emerging laboratory technologies and nontraditional testing workflow models, including next generation sequencing, biomarker testing, metagenomics, and others?

ASCP received comments from a number of our members focused on pathology informatics about the impact of the requirement that the pathologist sign-out must occur within a CLIA certified location. The comments we received argued that this requirement acts as a damper on the use and expansion of diagnostic telepathology services, and thus can delay patient care, limits the use of available technology, and increases the cost of providing these services. Our members argued that the location of the pathologist at the time of sign out has no direct bearing on the diagnosis rendered when using validated, accepted technology. Moreover, it was observed that given the decreasing number of pathologists at a time of expanding need for pathology services, telepathology could be an important mitigating strategy to eliminated delays in care do to resource restraints. We note that the specialty of radiology is not encumbered by a similar requirement, and, thus, are able to provide robust radiology services via telepathology nationally and internationally.

In addition, next generation sequencing and metagenomics are hypersensitive technologies that in addition to detecting bystander microbiota, detect sundry contaminants that are present in every pre-analytic phase of testing. Therefore, interpretation is absolutely key, as misinterpretation of bystander microbiota and/or contaminants as pathogens may lead to harm in that the misguided treatment may cause harm or the etiology of disease has not been detected and the disease process from the true pathogen will continue unabated. Guidance to ensure accuracy, reliability and reproducibility would help ensure quality patient care.

Question 3: What data are available that could assist in answering how CLIA may need to be revised or where guidance may be needed to ensure the accuracy and reliability of emerging technologies?

The College of American Pathologist (CAP) have addressed bioinformatics requirements in the Analytical Bioinformatics Process for the NGS section of the Molecular Pathology Checklist.

- Standards and Guidelines for Validating Next-Generation Sequencing Bioinformatics Pipelines: A Joint Recommendation of the Association for Molecular Pathology and the College of American Pathologist (https://doi.org/10.1016/j.jmoldx.2017.11.003)
- This year CLSI initiated committee in document development on Bioinformatics (MM25). Below is a list of current CLSI documents that may assist CLIA.
    - CLSI QMS01 ED5:2019 — A Quality Management System Model for Laboratory Services, 5th Edition
    - CLSI MM23 ED1:2015 — Molecular Diagnostic Methods for Solid Tumors (Nonhematological Neoplasms), 1st Edition
    - CLSI MM14 A2:2013 — Design of Molecular Proficiency Testing/External Quality Assessment, 2nd Edition
    - CLSI MM20 A:2012 — Quality Management for Molecular Genetic Testing, 1st Edition

It should also be noted that while there are some reports of misidentifications of pathogens by emerging technologies, the data on such misidentifications is scant. There are far more manuscripts demonstrating the potential of new technology providing diagnoses that could not otherwise be made. The data influencing the accuracy/reliability of the tests would come better from actually examining the results from well control clinical trials (e.g., performing metagenomics on specimens from patients without infection and demonstrating all the microbes that are detected).

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