CLIAC
Clinical Laboratory Improvement Advisory Committee

July 9, 2019

The Honorable Alex M. Azar II
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Azar:

I am writing on behalf of the Clinical Laboratory Improvement Advisory Committee (CLIAC) to express the Committee's recommendations regarding next generation sequencing.

During the April 10-11, 2018 CLIAC meeting, a recommendation was made to form a next generation sequencing workgroup to provide input to CLIAC for consideration in developing recommendations to CDC, CMS, and FDA, and to prioritize regulatory gaps for ensuring the quality of next generation sequencing in clinical laboratory settings. The Next Generation Sequencing Workgroup formed and met on January 16-17, 2019. The workgroup report was presented to CLIAC during the April 10-11, 2019 CLIAC meeting, resulting in eight CLIAC recommendations. The April 2019 meeting summary, including the workgroup report and presentation, can be found at https://www.cdc.gov/cliac/docs/summary/cliac0419_summary.pdf.

After deliberating on the how new technologies such as next generation sequencing fit into the current Clinical Laboratory Improvement Amendments of 1988 (CLIA) regulations, the need for new or updated next generation sequencing guidelines, and the incorporation of interoperability and data usage standards for clinical, genomic, and next generation sequencing testing, the Committee voted to provide the following recommendations to HHS.

1. CLIAC recommends that HHS thoroughly update the CLIA regulations to address issues related to new biomarker testing and other new technologies. This update may include a new section, revising existing sections, or other alternatives. This update should take account of the reports by the Personnel Regulations, Non-Traditional Workflow Models, and NGS workgroups presented to CLIAC. For NGS, such issues include but are not limited to, e.g., the definition, role, and responsibilities of bioinformaticists; quality control, e.g. moving from a simple requirement for

positive- and negative controls to controls more appropriate for NGS; establishment and verification of performance specifications, including the availability and sharing of samples; proficiency testing; reporting; delivery of data to patients, e.g. FASTQ vs. BAM vs. VCF-formatted NGS files; measurement, e.g. of NGS testing volumes; and data sharing, e.g. repositories and incentives and/or requirements for contribution to them.

2. CLIAC recommends that CMS, CDC, and FDA encourage professional societies and others (e.g. CLSI) to develop and/or update NGS guidelines. Specific fields of interest include, but are not limited to, oncology, inherited conditions, and microbiology applications of NGS. Recommended topics for guidelines include, but are not limited to:
   A. Revalidation of (i) analytical targets (e.g. additional genes or additional variant types); (ii) the bioinformatics pipeline (e.g. sequencing software updates, updates/changes in software in pipeline etc.)
   B. Data retention (e.g. file types, duration, intent)
   C. Data sharing (e.g. to patients, between organizations, between providers)

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

CLIAC is committed to providing HHS thoughtful advice related to clinical laboratory quality improvement and laboratory medicine practice. Thank you for your consideration.

If you have any questions regarding CLIAC's recommendation, please feel free to contact me via email at vang@alamedahealthsystem.org or by telephone at 510-437-4671.

Sincerely,

Valerie L. Ng, Ph.D., M.D.
Chairperson
Clinical Laboratory Improvement Advisory Committee (CLIAC)

cc:
Dr. Robert R. Redfield
Director, CDC

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