April 1, 2019

Centers for Medicare and Medicaid Services
Department of Health and Human Services
Attention: CMS
P.O. Box 8016
Baltimore, Maryland 21244

Dear Sir/Madam:

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to provide input to the Centers for Medicare and Medicaid Services (CMS) regarding its February 4, 2019 proposed rule, which would update the proficiency testing (PT) requirements under the Clinical Laboratory Improvement Amendments (CLIA). AACC supports the agency's efforts to modernize the PT regulations to reflect scientific advances in laboratory medicine over the past few decades.

Designated List of Analytes

Currently, CLIA requires clinical laboratories to demonstrate the accuracy of the laboratory tests they perform by enrolling in an approved PT program for each specialty, subspecialty, and analyte or test for which it is certified under CLIA. The current list of analytes for which a laboratory must enroll in PT has not been updated since 1992. Much has changed during that time.

CMS is proposing to expand the list to include troponin, hemoglobin A1c, and 27 other non-microbiology tests. AACC supports adding these tests to Subpart I of CLIA, as well five additional analytes: cyclosporine; everolimus; tacrolimus; sirolimus; and methotrexate. We further support the removal of ethosuximide, LDH isoenzymes, primidone, procainamide/NAPA, and quinidine from the list of analytes for which PT is required.

Changing to Percentage Acceptance Limits (AL)

CMS states that for several analytes *"there were no biological variability data because these analytes do not occur naturally in the body. Where there were such data, we used AL to get as close to, or below, an accuracy goal for the test that was based on biological variability data, and then we simulated several percentage based ALs to see if their results would have passed or failed at each simulation."*

AACC recommends that CMS conduct a pilot study that compares the existing AL criteria for the new analytes with the AL criteria based on biological variation to determine whether this is a valid approach. There is concern within the scientific community regarding the reliability of

biological variation data, since it sometimes overestimates the total allowable error when the experimental design and statistical analysis are not standardized (Clin Chem 2011; 57(9): 1334-1336).

We also want to note that ALs are not consistent with the Centers for Disease Control and Prevention (CDC) Laboratory Quality and Standardization Program goals. The CDC program and College of American Pathologists (CAP) accuracy-based surveys utilize commutable materials, while peer-group surveys utilize materials with unknown commutability characteristics. ALs that are directly traceable to accuracy-based programs may not be feasible, however at the least the ALs for testosterone and estradiol should be more closely aligned with the CDC Hormone Standardization program goals.

Target values

AACC supports the target values proposed by CMS for many of the analytes. However, we disagree with several of the agency's recommendations.

CMS recommends a target value of ± 20% for cholesterol, low density lipoprotein (direct measurement) (LDL cholesterol). The National Cholesterol Education Program (NCEP) advises laboratories to utilize methods with total error of ± 12%. AACC recommends that CMS adopt the NCEP total error goal for LDL cholesterol.

CMS is also proposing an acceptable range for hemoglobin A1c of ± 10%. This range differs from the current quality goal of CAP, which is set at ± 6%. We are concerned that broadening the acceptable range may have the effect of placing patients at risk of complications (microvascular disease and hypoglycemia) and an incorrect diagnosis of diabetes. AACC urges CMS to adopt a target value of ± 6% for hemoglobin A1c.

AACC also recommends that CMS set a target value of ± 20% for cyclosporine, everolimus, tacrolimus, sirolimus, and methotrexate. In addition, the association urges CMS to develop a process that ensures that future advancements in target values are quickly adopted and implemented.

On behalf of AACC, I would like to thank you for the opportunity to provide comments on this proposal. If you have any questions, please email Vince Stine, PhD, AACC's Senior Director of Government and Global Affairs, at vstine@aacc.org.

Sincerely,

Carmen L. Wiley, PhD, DABCC, FAACC
President, AACC