April 5, 2019

Centers for Medicare and Medicaid Services,
Department of Health and Human Services
Attention: CMS-3355-P
P.O. Box 8016
Baltimore, MD 21244-8016

RE: CMS-3355-P

The American Society for Microbiology (ASM) is grateful for the opportunity to comment on the proposed CLIA proficiency testing (PT) updates announced in the February 04 Federal Register. We request the following points of clarification in the relevant microbiology sections:

A. Proposed Changes to Microbiology PT

1. CATEGORIES OF TESTING

We are proposing to modify §§ 493.911 through 493.919 to remove the types of services listed for each microbiology subspecialty and to add the recommended categories of testing for each microbiology subspecialty as described in the bullets below. We believe that the revised microbiology PT regulations would better reflect current practices in microbiology.

Section 493.911(a): For bacteriology, we are proposing that the categories required include, as applicable:

- Gram stain including bacterial morphology;
- direct bacterial antigen detection;
- bacterial toxin detection;
- detection and identification of bacteria which includes one of the following:
  - Detection of growth or no growth in culture media or identification of bacteria to the highest level that the laboratory reports results on patient specimens;
  - and antimicrobial susceptibility or resistance testing on select bacteria.

“Resistance testing” is not a standard term, so we would like a definition added to the document. Is this referring to molecular testing for resistance genes? Or does the phrase “antimicrobial susceptibility” suffice? This is unclear without a definition.

Section 493.913(a): For mycobacteriology, we are proposing that the categories for which PT is required include, as applicable:

- Acid-fast stain;
- detection and identification of mycobacteria which includes one of the following:
  - Detection of growth or no growth in culture media or identification of mycobacteria;
  - and antimycobacterial susceptibility or resistance testing.

What method will be used for antimycobacterial susceptibility? Will it be \( rpoB \) testing? Which platform is expected to be used?

Section 493.915(a): For mycology, we are proposing that the categories for which PT is required include, as applicable:

- Direct fungal antigen detection; detection and identification of fungi and aerobic actinomycetes which includes one of the following:
o detection of growth or no growth in culture media or identification of fungi and aerobic actinomycetes;
o antifungal susceptibility or resistance testing.

There are no FDA-cleared methods for antifungal resistance testing, if we interpret the term resistance testing as resistance mechanism testing. Susceptibility testing encompasses both S and R result testing. Again, this is unclear without a definition of the term.

2. MAJOR GROUPS OF MICROORGANISMS

Require PT for a general list of types of organisms in each subspecialty. For example, in bacteriology, the groups listed should include Gram-neg. bacilli, gram-pos. bacilli, gram-neg cocci, and gram-pos cocci.

Therefore, we are proposing to remove the lists of specific example organisms from each microbiology subspecialty, §§ 493.911 through 493.919, and to add the following list of types of organisms to each.

§ 493.911(a)(3): For bacteriology, we are proposing that the annual program content must include representatives of the following major groups of medically important aerobic and anaerobic bacteria if appropriate for the sample sources: Gram-negative bacilli; gram-positive bacilli; gram-negative cocci; and gram-positive cocci. The more general list of types of organisms will continue to cover the six major groups of bacteria currently listed in the regulations.

We suggest that the list, as proposed, limits the organisms that can be used for PT. We suggest that, instead, the list read: gram-negative bacilli; gram-positive bacilli; gram-negative cocci or coccobacilli; and gram-positive cocci.

6. ANTIMICROBIAL SUSCEPTIBILITY TESTING

PT for antimicrobial susceptibility testing is currently required for bacteriology at § 493.911(b)(1) and mycobacteriology at § 493.913(b)(1), but it is not required for mycology, parasitology, or virology. Under the current regulations, some laboratories may perform the minimum required susceptibility testing on some organisms such as gram-positive cocci. When CLIAC discussed this issue, the point was made that by increasing the frequency and number of required susceptibility testing PT challenges for different groups of organisms, potential issues with patient testing in a laboratory may be detected sooner. CLIAC considered recommending increasing the susceptibility testing challenges to two per event and requiring one gram-positive and one gram-negative organism in each bacteriology testing event. CLIAC also considered whether PT should be required for resistance as well as susceptibility testing and whether these requirements should be extended to other microbiology subspecialties. Following this deliberation, CLIAC made the following recommendations:

- Required PT for antimicrobial susceptibility and/or resistance testing should be increased to two challenges per event for a total of six challenges per year in bacteriology and should include one gram-positive and one gram-negative organism in each event.
- PT should be required for laboratories that perform susceptibility and/or resistance testing in all microbiology subspecialties. It should include two challenges per event and should include resistant organisms.

In considering these recommendations, we reviewed the modules currently offered by PT programs that include susceptibility testing and noted that there is a limited number of applicable PT modules currently available for resistance testing. Also, no PT program currently offers applicable PT modules for antiparasitic susceptibility or resistance testing in the subspecialty of parasitology. We believe it could be beneficial to increase the number of
challenges per event from one to two for each microbiology subspecialty to increase the likelihood of detection of a problem in a laboratory.

PT for “resistance” is not well-defined. FDA has not approved any molecular test to predict patient treatment outcomes (i.e., resistance marker testing). Furthermore, CLSI has clear recommendations that resistance markers do not trump susceptibility testing. There are, to our knowledge, no resistance mechanism tests that are FDA cleared for fungi. Assessment of consensus between peer comparator groups as opposed to comparison of gold standard may be a flawed approach.

- **Section 493.915(a)(4):** For mycology, we are proposing to require at least two PT samples per event for susceptibility testing, including fungi that have a predetermined pattern of susceptibility to common antifungal agents.

Given the current status of mycology susceptibility testing, this action is premature. Problems include:

- Very few FDA cleared methods are available to detect resistance
- None of the FDA cleared methods apply FDA-recognized breakpoints (interpretive criteria)
- Extensive variability between test systems is evident in the current CAP surveys – *i.e.*, requiring additional testing will not serve a purpose if all results cannot be graded.

The ASM represents over 32,000 microbiologists professionally employed in a variety of settings related to the microbial sciences and many ASM members are involved in clinical laboratory medicine. These members direct clinical microbiology, immunology, and molecular diagnostic laboratories, are licensed or accredited to perform such testing, are industry representatives developing products for use, or are researchers involved in pre-market testing of laboratory diagnostics. ASM also includes clinician members involved in infectious disease prevention and management. As our clinical members are committed to providing healthcare of the highest quality we urge clear rules for proficiency testing that allow laboratories to follow an updated PT program without confusion.

Again, thank you for the opportunity to comment on these critical changes to the PT program.

Yours truly,

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