Clinical and Laboratory Standards Institute consensus procedures include an appeals process that is described in detail in Section 8 of the Administrative Procedures. For further information, contact CLSI or visit our website at www.clsi.org.

Summary of Comments and Subcommittee Responses

M100-S16, *Performance Standards for Antimicrobial Susceptibility Testing; Sixteenth Informational Supplement*

Tables 1 and 2B-4

1. In a recent CAP survey, participants were told that for *S. maltophilia,* they should have only reported results and interpretive breakpoints for the antimicrobial agents listed in Table 1. The question concerns minocycline, which is listed in the *S. maltophilia* column. Most laboratories can test tetracycline, but not minocycline. In footnote b in Table 1 (p. 94 in M100-S15), it states that tetracycline can be used to predict susceptibility (not I or R) to minocycline. Is the same statement true for *S. maltophilia*? There are no tetracycline breakpoints listed in the draft of Table 2B-4, *S. maltophilia* (M100-S16). If minocycline is not available on the AST medical device system the laboratory is using and the *S. maltophilia* isolate is susceptible to tetracycline, should the laboratories report the tetracycline result or not?

- **It is true that isolates of *S. maltophilia* that are susceptible to tetracycline are also susceptible to minocycline and doxycycline. However, >90% of *S. maltophilia* strains (personal communication, R. Jones, Sentry Antimicrobial Surveillance Program) are resistant to tetracycline but susceptible to minocycline and doxycycline, so testing tetracycline as a surrogate in place of the other tetracyclines is not recommended, because the vast majority of strains would be called resistant. When testing was done to determine criteria for testing *S. maltophilia* and *Burkholderia cepacia,* the CLSI working group chose to include only agents that were active, that were recommended by experts as therapies of these infections, and for which the recommended breakpoints were proven to be reproducible.**

Summary of Comments and Subcommittee Responses

M100-S17, *Performance Standards for Antimicrobial Susceptibility Testing; Seventeenth Informational Supplement*

General

1. Enterobacteriaceae and non-Enterobacteriaceae, which are resistant to tobramycin and amikacin, but susceptible to gentamicin, most likely produce a 6'-acetyltransferase. In this case, only one of the three gentamicin subcomponents, C_1, remains active. Since the fraction of C_1 varies between gentamicin formulations and C_1 appears to have different pharmacokinetics than gentamicin as a whole (*Antimicrob Agents Chemother*. 1975;7:328-332), are the gentamicin interpretive breakpoints accurate in these cases? Would it be reasonable to report gentamicin susceptibility as intermediate or provide a comment that gentamicin activity is uncertain?

- **The comment raises an interesting question. We have no data that would support changing the susceptible category to intermediate or resistant. However, when an isolate that is gentamicin susceptible and amikacin and tobramycin resistant is encountered and selective reporting is used by the laboratory, the susceptibility to gentamicin and the resistance to tobramycin and amikacin should all be reported.**

2. In CLSI document M2, the disk diffusion zone diameters are given with equivalent MIC breakpoints. In the overwhelming majority, they correspond to the MIC breakpoints printed in M7. However, some do not (eg, gentamicin and amikacin with Enterobacteriacea`e). Do you know why? Also, some of the MIC equivalent breakpoints are not in doubling dilutions (eg, in Table 2A, the S equivalent breakpoints are ≤ 12 μg/mL for netilmicin and ≤ 6 μg/mL for kanamycin). Why?

- **MIC equivalents listed in M2 represent the MIC breakpoints used when the zone size diameters were first determined. Since the M2 document was published before the M7 document, occasional discrepancies have existed and these mainly occur with the aminoglycosides. It is the intention of the subcommittee to reexamine these discrepancies in the near future.**

Summary of Comments and Subcommittee Responses

M100-S18, *Performance Standards for Antimicrobial Susceptibility Testing; Eighteenth Informational Supplement*

General

1. I am preparing to test MIC values and had a question about the dilutions. Someone mentioned to me that it is recommended to make only four dilutions from each antibiotic and then make a new standard at a lower concentration. I cannot find reference to that in my reading of M07. Would it be possible to do serial dilutions of the antibiotics rather than the method outlined in Table 6 of M100? I am concerned about being told that serial dilutions are only good for four dilutions because this is a standard practice I have always used to quantify CFU/mL and if it is not accurate with these antibiotic standards, then who is to say it is accurate for quantifying CFU/mL? And if it is accurate for quantifying CFU/mL, then why is it not accurate for quantifying MIC values for the antibiotics? Sorry for being confused. I have been handed a protocol already in place that seems to have a lot of unnecessary dilutions and testing being done to determine the MIC and am trying to scale it back.

- **In the experience of many of the subcommittee members who have been preparing reference dilution panels or plates for many years, they have never done what you describe, ie, prepare intermediate stock solutions when diluting more than four tubes. M07-A8 states in Section 10.4.1, "For the intermediate (10x) antimicrobial solutions, dilute the concentrated antimicrobial stock solution (see Section 7.3) as described in M100 Table 6 or by making serial twofold dilutions."**

2. Our pulmonologist has requested that we test *Staphylococcus* spp. and *Enterobacteriaceae* against moxifloxacin. The PharmD gave me a moxifloxacin product insert that gives different interpretive criteria (≥ 19 = susceptible) than those listed in M100 (≥ 24 mm = susceptible). Their product insert gives the same interpretive criteria for *Enterobacteriaceae,* and the CLSI document does not list ANY moxifloxacin interpretations for *Enterobacteriaceae.*

   I realize that we may use FDA or CLSI interpretive criteria, but the difference here is so great—19 mm would be RESISTANT per CLSI—that I don't feel comfortable reporting any results until I get a satisfactory explanation.

- **Although there are several reasons why the CLSI and FDA moxifloxacin breakpoints for staphylococci differ, the most important point for the laboratorian to understand is that CLSI breakpoints can be used for all staphylococci including MRSA, whereas the FDA breakpoints apply only to methicillin-susceptible staphylococci (per the FDA label for clinical use of the drug), so the laboratory should not report the drug on MRSA if using the FDA breakpoints. CLSI breakpoints for testing moxifloxacin with *Enterobacteriaceae* have not been determined, but FDA breakpoints are available for use. It is important to note that moxifloxacin is not approved for treatment of urinary tract infections due to low urinary concentrations and, thus, should not be tested on urinary isolates. The decision regarding which drugs to report for certain organism groups and which breakpoints to use should be made by the laboratory following discussions with appropriate stakeholders such as infectious disease practitioners and the pharmacy department, as well as the Pharmacy & Therapeutics and Infection Control committees of the medical staff. Clinical laboratories may implement newly approved or revised disk CLSI breakpoints as soon as they are published in M100. If a susceptibility testing device includes antimicrobial test concentrations sufficient to allow interpretation of susceptibility to**

an agent using the CLSI MIC breakpoints, a laboratory could, after appropriate validation, choose to interpret and report results using CLSI breakpoints.

3. What is the recommended frequency for quality control of various agar screening tests (eg, chromogenic media, vancomycin agar screen)?

- **Media containing antimicrobials used for primary isolation are not part of the scope of the susceptibility testing documents M02 and M07 (see CLSI document M22).**

  Single drug susceptibility tests/screens should be treated like other susceptibility tests (multiple concentrations or multiple drugs) until such time that recommendations and appropriate supportive data are available to streamline.

Table 2B-2

4. I am a microbiology supervisor with a question regarding interpretations for *Acinetobacter* to tigecycline. I have an infectious disease doctor complaining that this drug has been out for over a year, and still no interpretations and guidelines regarding this drug have been published. I have the 2008 standards and see this is true. Any time frame or information that you may have so that I could pass some pertinent information on to this doctor would be appreciated.

- **Interpretive criteria for tigecycline are not included in the CLSI documents for any genera because the drug manufacturer has not presented the necessary data for review by the subcommittee for subsequent publication of breakpoints in M100. In the meantime, one ordinarily could refer to the drug package insert for the US Food and Drug Administration (FDA) breakpoints; however, breakpoints for *Acinetobacter* are not included in the FDA list at this time because there is no clinical indication for tigecycline against *Acinetobacter*.**

5. CLSI document M100-S17 has MIC susceptibility ranges for colistin and polymyxin B against *Acinetobacter* sp. but there are no standards listed for disk diffusion on this isolate. Our Infectious Disease staff sometimes request that colistin and polymyxin B be tested against multidrug resistant (MDR) *Acinetobacter* isolates; and since these drugs are not available on our commercial conventional microdilution panels, I order these antimicrobials as (MIC) antibiotic gradient strips from a commercial source. The company, however, requires that a disclaimer be signed stating that we will use colistin and polymyxin B for INVESTIGATIONAL USE ONLY; a disclaimer is only good for six months and a new disclaimer must be signed for each new order. Should colistin and polymyxin B not be used for clinical purposes and are indeed for investigational use only?

- **There are no disk diffusion criteria for *Acinetobacter* in M100 because the disk test does not correlate with MIC tests and is therefore unreliable. Questions about the commercial gradient strip test should be addressed to the manufacturer. The use of colistin or polymyxin B for clinical treatment is a medical decision.**

Table 2G

6. I have a question about reporting cefepime (meningitis) and/or cefepime (nonmeningitis). In M100-S18 Table 2G, M07-MIC, cefepime (nonmeningitis) has a comment (11), "Only report interpretations for nonmeningitis and include the nonmeningitis notation on the report." There is not a US FDA-approved indication for the use of cefepime for meningitis. Just below the cefepime (nonmeningitis) entry, cefepime (meningitis) is listed with interpretative values. When would it be appropriate to use this?

- **The CLSI documents are also for use outside the United States where cefepime might be used for treatment of meningitis, which is the reason those criteria are included in Table 2G. Discuss with the Medical Director how to handle reporting of cefepime, but one solution in the United States might be to report only cefepime (nonmeningitis) with a note that cefepime is not US FDA-approved for treatment of meningitis.**