Revised July 2019

To: Recipients of M100, 29th ed.

From: Jennifer K. Adams, MT(ASCP), MSHA
Vice President, Standards and Quality

Subject: Combined Revisions

Revision: 10 July 2019

Revisions to Definitions

This notice is intended to inform users of revisions to two definitions in the Instructions for Use of Tables in CLSI document M100, Performance Standards for Antimicrobial Susceptibility Testing, 29th ed. The revisions are shown below as highlighted and/or stricken text.

**susceptible-dose dependent (SDD)** - a category defined by a breakpoint that implies that susceptibility of an isolate depends on the dosing regimen that is used in the patient. To achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either minimal inhibitory concentrations [MICs] or zone diameters) are in the SDD category, it is necessary to use a dosing regimen (ie, higher doses, more frequent doses, or both) that results in higher drug exposure than that achieved with the dose that was used to establish the susceptible breakpoint. Consideration should be given to the maximum, literature-supported dosage regimens, because higher exposure gives the highest probability of adequate coverage of an SDD isolate. Appendix E lists the doses used when establishing SDD categories. The drug label should be consulted for recommended doses and adjustment for organ function; **NOTE:** The concept of SDD has been included within the intermediate category definition for antimicrobial agents. However, this is often overlooked or not understood by clinicians and microbiologists when an intermediate result is reported. The SDD category may be assigned when doses well above those used to calculate the susceptible breakpoint are supported by the literature, widely used clinically, and/or approved and for which sufficient data to justify the designation exist and have been reviewed. The SDD category also includes a buffer zone for inherent variability in test methods, which should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins. **When the intermediate category is used, its definition remains unchanged.** See Appendix F for additional information.

**intermediate (I)** - a category defined by a breakpoint that includes isolates with MICs or zone diameters within the intermediate range that approach usually attainable blood and tissue levels and for which response rates may be lower than for susceptible isolates; **NOTE:** The intermediate category implies clinical efficacy in body sites where the drugs are physiologically concentrated or when a higher-than-normal dosage of a drug can be used. This category also includes a buffer zone for inherent variability in test methods, which should
prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins.

Please note, Tables 2 will be revised in M100, 30th ed. to appropriately indicate agents that have the potential to concentrate at an anatomical site. This information will also be included in the “intermediate” definition’s NOTE (eg, “NOTE: The intermediate category implies clinical efficacy in body sites where the drugs are physiologically concentrated. Agents in Tables 2 that have the potential to concentrate at an anatomical site are indicated. The intermediate category also includes a buffer zone for inherent variability in test methods, which should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins.”).

Revision: 13 March 2019

Daptomycin Breakpoint Revision

This notice is intended to inform users of a clinically important revision made to daptomycin breakpoints for Enterococcus spp. published in CLSI document M100, Performance Standards for Antimicrobial Susceptibility Testing, 29th ed.

During the 27-29 January 2019 meeting of the CLSI Subcommittee on Antimicrobial Susceptibility Testing, data were presented that warranted the approval of separate daptomycin breakpoints for Enterococcus faecium only and Enterococcus spp. (other than E. faecium). These revisions have been made in all electronic versions of M100, 29th ed. In addition, this memo has been provided to customers who have already received print copies and will be included with all print versions going forward. These revisions will be published in CLSI document M100, 30th ed.

Excerpts from Table 2D are included below. The first excerpt shows the daptomycin breakpoints as they were originally published in the 29th edition. The second excerpt shows the revised daptomycin breakpoints as they will be published in the upcoming 30th edition.

Updates to reflect these revisions were also made in the following locations:

- Overview of Changes
- CLSI Breakpoint Additions/Revisions Since 2010
- Appendix E

Table 2D. Zone Diameter and MIC Breakpoints for Enterococcus spp. (as originally published in 29th ed.)

The daptomycin breakpoints and associated comments for Enterococcus spp. as originally published in the 29th edition are shown in the Table 2D excerpt below.
<table>
<thead>
<tr>
<th>Test/Report Group</th>
<th>Antimicrobial Agent</th>
<th>Disk Content</th>
<th>Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm</th>
<th>Interpretive Categories and MIC Breakpoints, µg/mL</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>S : I : R</td>
<td>S : SDD : I : R</td>
<td></td>
</tr>
<tr>
<td>LIPOPEPTIDES</td>
<td>B</td>
<td>Daptomycin</td>
<td>-</td>
<td>-</td>
<td>1 ≤ 4 ≤ 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>E. faecium only</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Daptomycin</td>
<td>-</td>
<td>-</td>
<td>2 ≤ 4 ≤ 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Enterococcus</em> spp. (other than <em>E. faecium</em>)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>&lt; 2 ≥ 4 ≥ 8</td>
<td></td>
</tr>
</tbody>
</table>

Table 2D. Zone Diameter and MIC Breakpoints for *Enterococcus* spp. (revised, to be published in upcoming 30th ed.)

The revised daptomycin breakpoints and associated comments are shown in the revised Table 2D excerpt below. All revisions are highlighted.

If you require any additional clarification regarding these revisions, please contact CLSI Customer Service (customerservice@clsi.org).

We appreciate your commitment to CLSI and regret any inconvenience.