

10 July 2019

To: Recipients of M100, 29th ed.

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Subject: 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~~ ~~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.

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.”).

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.