Table 2H-2. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. Viridans Group

Testing Conditions

Medium: Disk diffusion: MHA with 5% sheep blood
Broth dilution: CAMHB with LHB (2.5% to 5% v/v); the CAMHB should be supplemented to 50 µg/mL calcium for daptomycin (see M07[1] for instructions for preparation of LHB)
Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.

Inoculum: Colony suspension, equivalent to a 0.5 McFarland standard using colonies from an overnight (18- to 20-hour) sheep blood agar plate

Incubation: 35°C ± 2°C
Disk diffusion: 5% CO_2; 20–24 hours
Dilution methods: ambient air; 20–24 hours (CO_2 if necessary for growth with agar dilution)

Routine QC Recommendations (see Tables 4B and 5B for acceptable QC ranges)

S. pneumoniae ATCC®[a] 49619

When a commercial test system is used for susceptibility testing, refer to the manufacturer's instructions for QC test recommendations and QC ranges.

General Comments

(1) Refer to Table 1N for antimicrobial agents that should be considered for testing and reporting by microbiology laboratories.

(2) For disk diffusion, measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Do not measure the zone of inhibition of hemolysis. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth.

(3) For viridans streptococci when testing chloramphenicol, clindamycin, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored (see M07,[1] Figures 3 and 4).

(4) The viridans group of streptococci includes the following five groups, with several species within each group: *mutans* group, *salivarius* group, *bovis* group, *anginosus* group (previously *S. milleri* group), and *mitis* group. The *anginosus* group includes small colony-forming β-hemolytic strains with groups A, C, F, and G antigens. For detailed information on the species within the groups, please refer to recent literature.

(5) Breakpoints for *Streptococcus* spp. viridans group are proposed based on population distributions of various species, pharmacokinetics of the antimicrobial agents, previously published literature, and the clinical experience of subcommittee members. Systematically collected clinical data were not available for review with many of the antimicrobial agents in this table.

NOTE: Information in black boldface type is new or modified since the previous edition.

Table 2H-2. *Streptococcus* spp. Viridans Group (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	S	I	R	
PENICILLINS								
Penicillin	-	-	-	-	≤0.12	0.25-2	≥4	**(6)** Viridans streptococci isolated from normally sterile anatomical sites (eg, CSF, blood, bone) should be tested for penicillin susceptibility using an MIC method. **(7)** A penicillin MIC of ≤0.125 µg/mL is the same as a penicillin MIC of ≤0.12 µg/mL and both should be interpreted as susceptible. Laboratories should report an MIC of ≤0.125 µg/mL as ≤0.12 µg/mL. **(8)** ***Rx:*** Penicillin- or ampicillin-intermediate isolates may necessitate combined therapy with an aminoglycoside for bactericidal action.
Ampicillin					≤0.25	0.5-4	≥8	
β-LACTAM COMBINATION AGENTS								
Ceftolozane-tazobactam	-	-	-	-	≤8/4	16/4	≥32/4	**(9)** Breakpoints are based on a dosage regimen of 1.5 g administered every 8 h.
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)								
Cefepime	30 µg	≥24	22-23	≤21	≤1	2	≥4	
Cefotaxime	30 µg	≥28	26-27	≤25	≤1	2	≥4	
Ceftriaxone	30 µg	≥27	25-26	≤24	≤1	2	≥4	
CARBAPENEMS								
Doripenem*	-	-	-	-	≤1	-	-	
Ertapenem*	-	-	-	-	≤1	-	-	
Meropenem*	-	-	-	-	≤0.5	-	-	
GLYCOPEPTIDES								
Vancomycin	30 µg	≥17	-	-	≤1	-	-	

Table 2H-2. *Streptococcus* spp. Viridans Group (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	S	I	R	
LIPOGLYCOPEPTIDES								
Dalbavancin	-	-	-	-	≤0.25	-	-	**(10)** Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes. **(11) Report only on** *S. anginosus* group (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*).
Oritavancin	-	-	-	-	≤0.25	-	-	**(12)** Breakpoints are based on a dosage regimen of 1200 mg IV administered once.
Telavancin	-	-	-	-	≤0.06	-	-	**(13)** Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h.
LIPOPEPTIDES								
Daptomycin*	-	-	-	-	≤1	-	-	**(14) Not routinely** reported **on organisms isolated** from the respiratory tract.
MACROLIDES								
(15) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. **(16)** Not routinely reported on **organisms isolated** from the urinary tract.								
Erythromycin	15 µg	≥21	16-20	≤15	≤0.25	0.5	≥1	
Azithromycin*	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
Clarithromycin*	15 µg	≥21	17-20	≤16	≤0.25	0.5	≥1	
Dirithromycin*	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
TETRACYCLINES								
(17) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, resistance to doxycycline and minocycline cannot be inferred from tetracycline resistance.								
Tetracycline*	30 µg	≥23	19-22	≤18	≤2	4	≥8	
FLUOROQUINOLONES								
Levofloxacin	5 µg	≥17	14-16	≤13	≤2	4	≥8	
Ofloxacin*	5 µg	≥16	13-15	≤12	≤2	4	≥8	
Gatifloxacin*	5 µg	≥21	18-20	≤17	≤1	2	≥4	
Grepafloxacin*	5 µg	≥19	16-18	≤15	≤0.5	1	≥2	
Trovafloxacin*	10 µg	≥19	16-18	≤15	≤1	2	≥4	

Table 2H-2. *Streptococcus* spp. Viridans Group (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	S	I	R	
PHENICOLS								
Chloramphenicol*****	30 µg	≥21	18-20	≤17	≤4	8	≥16	See comment (16).
LINCOSAMIDES								
Clindamycin	2 µg	≥19	16-18	≤15	≤0.25	0.5	≥1	See comment (16).
STREPTOGRAMINS								
Quinupristin-dalfopristin*****	15 µg	≥19	16-18	≤15	≤1	2	≥4	
OXAZOLIDINONES								
(18) *S. anginosus* group that test susceptible to linezolid by MIC are also considered susceptible to tedizolid. However, some organisms that are nonsusceptible to linezolid may be susceptible to tedizolid.								
Linezolid	30 µg	≥21	-	-	≤2	-	-	
Tedizolid	-	-	-	-	≤0.25	-	-	**(19)** Breakpoints are based on a dosage regimen of 200 mg administered every 24 h. See comment (11).

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CSF, cerebrospinal fluid; I, intermediate; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Symbol: *, designation for "Other" agents that are not included in Tables 1 but have established clinical breakpoints.

<u>Footnote</u>

a. ATCC® is a registered trademark of the American Type Culture Collection.

Reference for Table 2H-2

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.