Table 2H-1. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. β-Hemolytic 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.

Refer to Table 3I for additional testing recommendations, reporting suggestions, and QC.

General Comments

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

(2) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk (see the *M02 Disk Diffusion Reading Guide*[2]). 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 β-hemolytic 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) For this table, the β-hemolytic group includes the large colony-forming pyogenic strains of streptococci with group A (*S. pyogenes*), C, or G antigens and strains with Group B (*S. agalactiae*) antigen. Small colony-forming β-hemolytic strains with group A, C, F, or G antigens (*S. anginosus* group, previously *S. milleri*) are considered part of the viridans group, and breakpoints for the viridans group should be used (see Table 2H-2).

Table 2H-1. *Streptococcus* spp. ß-Hemolytic Group (Continued)

(5) Penicillin and ampicillin are drugs of choice for treatment of ß-hemolytic streptococcal infections. Susceptibility testing of penicillins and other ß-lactams approved by the US Food and Drug Administration for treatment of ß-hemolytic streptococcal infections does not need to be performed routinely, because nonsusceptible isolates (ie, penicillin MICs > 0.12 and ampicillin MICs > 0.25 µg/mL) are extremely rare in any ß-hemolytic streptococcus and have not been reported for *S. pyogenes*. If testing is performed, any ß-hemolytic streptococcal isolate found to be nonsusceptible should be re-identified, retested, and, if confirmed, submitted to a public health laboratory. See Appendix A for additional instructions.

(6) Breakpoints for *Streptococcus* spp. ß-hemolytic 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-1. *Streptococcus* spp. ß-Hemolytic 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								
(7) An organism that is susceptible to penicillin can be considered susceptible to antimicrobial agents listed here when used for approved indications and does not need to be tested against those agents. For groups A, B, C, and G ß-hemolytic streptococci, penicillin is tested as a surrogate for ampicillin, amoxicillin, amoxicillin-clavulanate, ampicillin-sulbactam, cefazolin, cefepime, ceftaroline, cephradine, cephalothin, cefotaxime, ceftriaxone, ceftizoxime, imipenem, ertapenem, and meropenem. For group A ß-hemolytic streptococci, penicillin is also a surrogate for cefaclor, cefdinir, cefprozil, ceftibuten, cefuroxime, and cefpodoxime.							
Penicillin or ampicillin	10 units 10 µg	≥24 ≥24	- -	- -	≤0.12 ≤0.25	- -	- -	See general comment (5).
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)								
See comment (7).								
Cefepime or cefotaxime or ceftriaxone	30 µg 30 µg 30 µg	≥24 ≥24 ≥24	- - -	- - -	≤0.5 ≤0.5 ≤0.5	- - -	- - -	
Ceftaroline	30 µg	≥26	-	-	≤0.5	-	-	**(8)** Breakpoints are based on a dosage regimen of 600 mg administered every 12 h.
CARBAPENEMS								
See comment (7).								
Doripenem*	-	-	-	-	≤0.12	-	-	
Ertapenem*	-	-	-	-	≤1	-	-	
Meropenem*	-	-	-	-	≤0.5	-	-	
GLYCOPEPTIDES								
Vancomycin	30 µg	≥17	-	-	≤1	-	-	
LIPOGLYCOPEPTIDES								
Dalbavancin	-	-	-	-	≤0.25	-	-	**(9) Report only on** *S. pyogenes*, *S. agalactiae*, and *S. dysgalactiae*. **(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.
Oritavancin	-	-	-	-	≤0.25	-	-	**(11)** Breakpoints are based on a dosage regimen of 1200 mg IV administered once.
Telavancin	-	-	-	-	≤0.12	-	-	**(12)** Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h.
LIPOPEPTIDES								
Daptomycin	-	-	-	-	≤1	-	-	**(13) Not routinely** reported **on organisms isolated** from the respiratory tract.

Table 2H-1. *Streptococcus* spp. β-Hemolytic 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	
MACROLIDES								
(14) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. **(15)** Not routinely reported on **organisms isolated** from the urinary tract.								
Erythromycin	15 µg	≥21	16-20	≤15	≤0.25	0.5	≥1	**(16)** ***Rx:*** Recommendations for intrapartum prophylaxis for group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin. Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin, but may be resistant to erythromycin and clindamycin. When a group B *Streptococcus* is isolated from a pregnant woman with severe penicillin allergy (high risk for anaphylaxis), erythromycin and clindamycin (including ICR) should be tested, and only clindamycin should be reported. Erythromycin should be tested for ICR determination only and should not be reported. See Table 3I.
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	
Gatifloxacin*	5 µg	≥21	18-20	≤17	≤1	2	≥4	
Grepafloxacin*	5 µg	≥19	16-18	≤15	≤0.5	1	≥2	
Ofloxacin*	5 µg	≥16	13-15	≤12	≤2	4	≥8	
Trovafloxacin*	10 µg	≥19	16-18	≤15	≤1	2	≥4	
PHENICOLS								
Chloramphenicol*	30 µg	≥21	18-20	≤17	≤4	8	≥16	See comment (15).

Table 2H-1. *Streptococcus* spp. ß-Hemolytic 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	
LINCOSAMIDES								
Clindamycin	2 µg	≥19	16-18	≤15	≤0.25	0.5	≥1	See comments (15) and (16). **(18)** For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for ICR by disk diffusion using the D-zone test or by broth microdilution is required before reporting clindamycin. See Table 3I, Subchapter 3.9 in M02,[3] and Subchapter 3.12 in M07.[1]
STREPTOGRAMINS								
Quinupristin-dalfopristin*	15 µg	≥19	16-18	≤15	≤1	2	≥4	**(19)** For reporting against *S. pyogenes* only.
OXAZOLIDINONES								
(20) *S. agalactiae* and *S. pyogenes* 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	-	-	-	-	≤0.5	-	-	**(21) Report only on** *S. pyogenes* and *S. agalactiae*. **(22)** Breakpoints are based on a dosage regimen of 200 mg administered every 24 h.

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; ICR, inducible clindamycin resistance; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.
Symbol: *, designation for "Other" agents not included in Tables 1 but have established clinical breakpoints.

Footnote

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

References for Table 2H-1

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

2 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.