Table 2G. Zone Diameter and MIC Breakpoints for *Streptococcus pneumoniae*

Testing Conditions

Medium: Disk diffusion: MHA with 5% sheep blood or MH-F agar (MHA with 5% defibrinated horse blood and 20 µg/mL NAD)
Broth dilution: CAMHB with LHB (2.5% to 5% v/v) (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, prepared 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

Disk diffusion: deterioration of oxacillin disk content is best assessed with *S. aureus* ATCC® 25923, with an acceptable range of 18–24 mm on unsupplemented MHA.

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) 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. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

(2) For pneumococci 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). With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, read the end point at the concentration in which there is ≥ 80% reduction in growth compared with the control (see M07,[1] Figure 5).

(3) Amoxicillin, ampicillin, cefepime, cefotaxime, ceftriaxone, cefuroxime, ertapenem, imipenem, and meropenem may be used to treat pneumococcal infections; however, reliable disk diffusion susceptibility tests with these agents do not yet exist. The *in vitro* activity of these agents is best determined using an MIC method.

(4) For *S. pneumoniae* isolated from CSF, penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method (such as that described in M07[1]) and reported routinely. Such isolates can also be tested against vancomycin using the MIC or disk diffusion method.

(5) For disk diffusion, results using MHA with 5% sheep blood and MH-F agar were equivalent when disk contents, testing conditions, and zone diameter breakpoints in Table 2G were used. Disk diffusion QC ranges for *S. pneumoniae* ATCC® 49619 in Table 4B apply to testing using either MHA with 5% sheep blood or MH-F agar.

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	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									
6) For nonmeningitis isolates, a penicillin MIC of ≤ 0.06 µg/mL (or oxacillin zone ≥ 20 mm) can predict susceptibility to the following β-lactams: ampicillin (oral or parenteral), ampicillin-sulbactam, amoxicillin, amoxicillin-clavulanate, cefaclor, cefdinir, cefditoren, cefepime, cefotaxime, cefpodoxime, cefprozil, ceftaroline, ceftizoxime, ceftriaxone, cefuroxime, doripenem, ertapenem, imipenem, loracarbef, meropenem. See general comment (4).									
A	Penicillin	1 µg oxacillin	≥ 20	-	-	-	-	-	**(7)** Isolates of pneumococci with oxacillin zone sizes ≥ 20 mm are susceptible (MIC ≤ 0.06 µg/mL) to penicillin. Penicillin and cefotaxime, ceftriaxone, or meropenem MICs should be determined for isolates with oxacillin zone diameters ≤ 19 mm, because zones ≤ 19 mm occur with penicillin-resistant, -intermediate, or certain -susceptible strains. For isolates with oxacillin zones ≤ 19 mm, do not report penicillin as resistant without performing a penicillin MIC test.
A	Penicillin parenteral (nonmeningitis)	-	-	-	-	≤ 2	4	≥ 8	**(8)** ***Rx:*** Doses of intravenous penicillin of at least 2 million units every 4 hours in adults with normal renal function (12 million units per day) can be used to treat nonmeningeal pneumococcal infections due to strains with penicillin MICs ≤ 2 µg/mL. Strains with an intermediate MIC of 4 µg/mL may necessitate penicillin doses of 18–24 million units per day. **(9)** For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.
A	Penicillin parenteral (meningitis)	-	-	-	-	≤ 0.06	-	≥ 0.12	**(10)** ***Rx:*** Use of penicillin in meningitis requires therapy with maximum doses of intravenous penicillin (eg, at least 3 million units every 4 hours in adults with normal renal function). **(11)** For CSF isolates, report only meningitis interpretations. See general comment (4).

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	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 (Continued)									
A	Penicillin (oral penicillin V)	-	-	-	-	≤0.06	0.12-1	≥2	**(12)** Interpretations for oral penicillin may be reported for isolates other than those from CSF.
C	Amoxicillin (nonmeningitis)	-	-	-	-	≤2	4	≥8	
C	Amoxicillin-clavulanate (nonmeningitis)					≤2/1	4/2	≥8/4	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
See comment (6).									
O	Cefepime (meningitis)	-	-	-	-	≤0.5	1	≥2	**(13)** In the United States, for CSF isolates, report only nonmeningitis interpretations. There is not an FDA-approved indication for the use of cefepime for meningitis in the United States.
B	Cefepime (nonmeningitis)	-	-	-	-	≤1	2	≥4	**(14)** In the United States, report only interpretations for nonmeningitis and include the nonmeningitis notation on the report.
B	Cefotaxime (meningitis)	-	-	-	-	≤0.5	1	≥2	**(15)** For CSF isolates, report only meningitis interpretations. **(16)** ***Rx:*** Use of cefotaxime or ceftriaxone in meningitis requires therapy with maximum doses. See general comment (4).
B	Ceftriaxone (meningitis)	-	-	-	-	≤0.5	1	≥2	

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	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	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)									
B B	Cefotaxime (nonmeningitis) Ceftriaxone (nonmeningitis)	- -	- -	- -	- -	≤1 ≤1	2 2	≥4 ≥4	**(17)** For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.
C	Ceftaroline (nonmeningitis)	30 µg	≥26	-	-	≤0.5	-	-	**(18)** Breakpoints are based on a dosage regimen of 600 mg administered every 12 h.
C	Cefuroxime (parenteral)	-	-	-	-	≤0.5	1	≥2	
CEPHEMS (ORAL)									
See comment (6).									
C	Cefuroxime (oral)	-	-	-	-	≤1	2	≥4	**(19)** Interpretations for oral cefuroxime may be reported for isolates other than those from CSF.
O	Cefaclor	-	-	-	-	≤1	2	≥4	
O	Cefdinir	-	-	-	-	≤0.5	1	≥2	
O	Cefpodoxime	-	-	-	-	≤0.5	1	≥2	
O	Cefprozil	-	-	-	-	≤2	4	≥8	
O	Loracarbef	-	-	-	-	≤2	4	≥8	
CARBAPENEMS									
See comment (6).									
B	Meropenem	-	-	-	-	≤0.25	0.5	≥1	See general comment (4) and comment (7).
C	Ertapenem	-	-	-	-	≤1	2	≥4	
C	Imipenem	-	-	-	-	≤0.12	0.25-0.5	≥1	
O	Doripenem	-	-	-	-	≤1	-	-	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	-	-	≤1	-	-	See general comment (4).
MACROLIDES									
(20) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. **(21)** Not routinely reported for organisms isolated from the urinary tract.									
A	Erythromycin	15 µg	≥21	16-20	≤15	≤0.25	0.5	≥1	
O	Azithromycin	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
O	Clarithromycin	15 µg	≥21	17-20	≤16	≤0.25	0.5	≥1	
O	Dirithromycin	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
TETRACYCLINES									
(22) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline. However, resistance to doxycycline cannot be inferred from tetracycline resistance.									
B B	Tetracycline Doxycycline	30 µg 30 µg	≥28 ≥28	25-27 25-27	≤24 ≤24	≤1 ≤0.25	2 0.5	≥4 ≥1	

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	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	
FLUOROQUINOLONES									
B B B	Gemifloxacin Levofloxacin Moxifloxacin	5 µg 5 µg 5 µg	≥23 ≥17 ≥18	20-22 14-16 15-17	≤19 ≤13 ≤14	≤0.12 ≤2 ≤1	0.25 4 2	≥0.5 ≥8 ≥4	**(23)** *S. pneumoniae* isolates susceptible to levofloxacin are predictably susceptible to gemifloxacin and moxifloxacin. However, *S. pneumoniae* susceptible to gemifloxacin or moxifloxacin cannot be assumed to be susceptible to levofloxacin.
O	Gatifloxacin	5 µg	≥21	18-20	≤17	≤1	2	≥4	
O	Ofloxacin	5 µg	≥16	13-15	≤12	≤2	4	≥8	
O	Sparfloxacin	5 µg	≥19	16-18	≤15	≤0.5	1	≥2	
FOLATE PATHWAY ANTAGONISTS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥19	16-18	≤15	≤0.5/9.5	1/19-2/38	≥4/76	
PHENICOLS									
C	Chloramphenicol	30 µg	≥21	-	≤20	≤4	-	≥8	See comment (21).
ANSAMYCINS									
C	Rifampin	5 µg	≥19	17-18	≤16	≤1	2	≥4	**(24)** ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.
LINCOSAMIDES									
B	Clindamycin	2 µg	≥19	16-18	≤15	≤0.25	0.5	≥1	**(25)** 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]). See comment (21).
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16-18	≤15	≤1	2	≥4	
OXAZOLIDINONES									
C	Linezolid	30 µg	≥21	-	-	≤2	-	-	
PLEUROMUTILINS									
B	**Lefamulin**	**20 µg**	**≥17**	**-**	**-**	**≤0.5**	**-**	**-**	**(26) The susceptible breakpoints are based on a dosage regimen of 150 mg IV or 600 mg orally administered every 12 h.** **(27) Not routinely reported on organisms isolated from the urinary tract.**

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CSF, cerebrospinal fluid; FDA, US Food and Drug Administration; I, intermediate; ICR, inducible clindamycin resistance; IV, intravenous; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MH-F agar, Mueller-Hinton fastidious agar; MIC, minimal inhibitory concentration; NAD, ß-nicotinamide adenine dinucleotide; QC, quality control; R, resistant; S, susceptible.

Table 2G. *Streptococcus pneumoniae* (Continued)

Footnote

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

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

References for Table 2G

[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.