Table 1G. *Streptococcus pneumoniae*

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Erythromycin[a,b]			
Penicillin[c]			Amoxicillin[d] Amoxicillin-clavulanate[d]
Trimethoprim-sulfamethoxazole			
Cefotaxime[c,d] Ceftriaxone[c,d]			Cefepime[d]
			Ceftaroline
	Meropenem[c,d]		Ertapenem[d] Imipenem[d]
	Clindamycin[b]		
	Doxycycline Tetracycline		
	Levofloxacin[e] Moxifloxacin[e]		
	Vancomycin[c]		
			Lefamulin[b]
			Linezolid
			Cefuroxime[d]
			Rifampin[f]

Abbreviations: CSF, cerebrospinal fluid; MDRO, multidrug-resistant organism; MIC, minimal inhibitory concentration.

Table 1G. *Streptococcus pneumoniae* (Continued)

Footnotes

a. Susceptibility and resistance to azithromycin and clarithromycin can be predicted by testing erythromycin.

b. Not routinely reported on organisms isolated from the urinary tract.

c. Penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method (such as that described in CLSI M07[1]) and reported routinely with *S. pneumoniae* isolated from CSF. Such isolates can also be tested against vancomycin using the MIC or disk diffusion method. With isolates from other sites, the oxacillin disk test may be used. If the oxacillin zone size is ≤ 19 mm, cefotaxime, ceftriaxone, meropenem, or penicillin MICs should be determined.

d. MIC testing only; disk diffusion test is unreliable.

e. Organisms that are susceptible to levofloxacin are also considered susceptible to gemifloxacin and moxifloxacin. However, some organisms that are intermediate or resistant to levofloxacin may be susceptible to gemifloxacin, moxifloxacin, or both.

f. ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.

Reference for Table 1G

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically.* 12th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2024.

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% mechanically defibrinated horse blood and 20 µg/mL NAD) Broth dilution: CAMHB with LHB (2.5% to 5% v/v) (see CLSI 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)

QC Recommendations

Refer to the following:

- **Tables 4B and 5B that list acceptable QC ranges applicable for each method**
- **Appendix I to develop a QC plan**

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

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

General Comments

(1) Refer to Table 1G 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 CLSI M02QG[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.

Table 2G. *Streptococcus pneumoniae* (Continued)

(3) 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 CLSI M07[1]). 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 CLSI M07[1]).

(4) 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.

(5) Penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method (such as that described in CLSI M07[1]) and reported routinely with *S. pneumoniae* isolated from CSF. Such isolates can also be tested against vancomycin using the MIC or disk diffusion method. With isolates from other sites, the oxacillin disk test may be used. If the oxacillin zone size is ≤ 19 mm, cefotaxime, ceftriaxone, meropenem, or penicillin MICs should be determined.

(6) 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 this table were used. Disk diffusion QC ranges for *S. pneumoniae* ATCC®[a] 49619 in Table 4B apply to testing using either MHA with 5% sheep blood or MH-F agar.

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

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) 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 (5).								
Penicillin	1 µg oxacillin	≥ 20	–	–	–	–	–	**(8)** 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.

Table 2G. *Streptococcus pneumoniae* (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 (Continued)								
Penicillin parenteral (nonmeningitis)	–	–	–	–	≤ 2	4	≥ 8	**(9)** For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.
Penicillin parenteral (meningitis)	–	–	–	–	≤ 0.06	–	≥ 0.12	**(10)** For CSF isolates, report only meningitis interpretations. See general comment (5).
Penicillin (oral penicillin V)	–	–	–	–	≤ 0.06	0.12–1	≥ 2	**(11)** Interpretations for oral penicillin may be reported for isolates other than those from CSF.
Amoxicillin (nonmeningitis) Amoxicillin-clavulanate (nonmeningitis)	–	–	–	–	≤ 2 ≤ 2/1	4 4/2	≥ 8 ≥ 8/4	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)								
See comment (7).								
Cefepime (meningitis)*	–	–	–	–	≤ 0.5	1	≥ 2	**(12)** 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.
Cefepime (nonmeningitis)	–	–	–	–	≤ 1	2	≥ 4	**(13)** In the United States, report only interpretations for nonmeningitis and include the nonmeningitis notation on the report.
Cefotaxime (meningitis) Ceftriaxone (meningitis)	– –	– –	– –	– –	≤ 0.5 ≤ 0.5	1 1	≥ 2 ≥ 2	**(14)** For CSF isolates, report only meningitis interpretations. **(15) *Rx:*** Use of cefotaxime or ceftriaxone in meningitis requires therapy with maximum doses. See general comment (5).
Cefotaxime (nonmeningitis) Ceftriaxone (nonmeningitis)	– –	– –	– –	– –	≤ 1 ≤ 1	2 2	≥ 4 ≥ 4	**(16)** For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.

Table 2G. *Streptococcus pneumoniae* (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	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)								
Ceftaroline (nonmeningitis)	30 µg	≥ 26	–	–	≤ 0.5	–	–	
Cefuroxime (parenteral)	–	–	–	–	≤ 0.5	1	≥ 2	
CEPHEMS (ORAL)								
See comment (7).								
Cefuroxime (oral)	–	–	–	–	≤ 1	2	≥ 4	**(17)** Interpretations for oral cefuroxime may be reported for isolates other than those from CSF.
Cefaclor*	–	–	–	–	≤ 1	2	≥ 4	
Cefdinir*	–	–	–	–	≤ 0.5	1	≥ 2	
Cefpodoxime*	–	–	–	–	≤ 0.5	1	≥ 2	
Cefprozil*	–	–	–	–	≤ 2	4	≥ 8	
Loracarbef*	–	–	–	–	≤ 2	4	≥ 8	
CARBAPENEMS								
See comment (7).								
Meropenem	–	–	–	–	≤ 0.25	0.5	≥ 1	See general comment (5) and comment (8).
Ertapenem	–	–	–	–	≤ 1	2	≥ 4	
Imipenem	–	–	–	–	≤ 0.12	0.25–0.5	≥ 1	
Doripenem*	–	–	–	–	≤ 1	–	–	
GLYCOPEPTIDES								
Vancomycin	30 µg	≥ 17	–	–	≤ 1	–	–	See general comment (5).
MACROLIDES								
(18) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. **(19)** 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	

Table 2G. *Streptococcus pneumoniae* (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	
TETRACYCLINES								
(20) Isolates that **test** susceptible to tetracycline are considered susceptible to doxycycline. **Isolates that test intermediate or resistant to tetracycline should be tested against doxycycline if that result is needed for treatment.**								
Tetracycline	30 µg	≥ 28	25–27	≤ 24	≤ 1	2	≥ 4	
Doxycycline	30 µg	≥ 28	25–27	≤ 24	≤ 0.25	0.5	≥ 1	
FLUOROQUINOLONES								
Gemifloxacin*	5 µg	≥ 23	20–22	≤ 19	≤ 0.12	0.25	≥ 0.5	**(21)** Organisms that are susceptible to levofloxacin are also considered susceptible to gemifloxacin and moxifloxacin. However, some organisms that are intermediate or resistant to levofloxacin may be susceptible to gemifloxacin, moxifloxacin, or both.
Levofloxacin	5 µg	≥ 17	14–16	≤ 13	≤ 2	4	≥ 8	
Moxifloxacin	5 µg	≥ 18	15–17	≤ 14	≤ 1	2	≥ 4	
Gatifloxacin*	5 µg	≥ 21	18–20	≤ 17	≤ 1	2	≥ 4	
Ofloxacin*	5 µg	≥ 16	13–15	≤ 12	≤ 2	4	≥ 8	
Sparfloxacin*	5 µg	≥ 19	16–18	≤ 15	≤ 0.5	1	≥ 2	
FOLATE PATHWAY ANTAGONISTS								
Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥ 19	16–18	≤ 15	≤ 0.5/9.5	1/19–2/38	≥ 4/76	
PHENICOLS								
Chloramphenicol*	30 µg	≥ 21	–	≤ 20	≤ 4	–	≥ 8	See comment (19).
ANSAMYCINS								
Rifampin	5 µg	≥ 19	17–18	≤ 16	≤ 1	2	≥ 4	**(22) *Rx:*** Rifampin should not be used alone for antimicrobial therapy.
LINCOSAMIDES								
Clindamycin	2 µg	≥ 19	16–18	≤ 15	≤ 0.25	0.5	≥ 1	**(23)** 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 3J, CLSI M02,[3] and CLSI M07[1]). See comment (19).

Table 2G. *Streptococcus pneumoniae* (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	
STREPTOGRAMINS								
Quinupristin-dalfopristin*	15 µg	≥ 19	16–18	≤ 15	≤ 1	2	≥ 4	
OXAZOLIDINONES								
Linezolid	30 µg	≥ 21	–	–	≤ 2	–	–	
PLEUROMUTILINS								
Lefamulin	20 µg	≥ 19	–		≤ 0.5	–	–	See comment (19).

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CO_2, carbon dioxide; CSF, cerebrospinal fluid; FDA, US Food and Drug Administration; I, intermediate; ICR, inducible clindamycin resistance; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MH-F, Mueller-Hinton fastidious; MIC, minimal inhibitory concentration; NAD, β-nicotinamide adenine dinucleotide; QC, quality control; R, resistant; S, susceptible.
Symbol: *, designation for "Other" agents that are 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 2G

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically.* 12th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2024.

2 CLSI. *M02 Disk Diffusion Reading Guide.* 2nd ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2024.

3 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests.* 14th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2024.