The Challenge of Antimicrobial Susceptibility Testing in EQAP Round 45

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M100

Performance Standards for Antimicrobial Susceptibility Testing

This document includes updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02, M07, and M11.

A CLSI supplement for global application.

Overview of Changes

M100-Ed33 replaces the previous edition of the supplement, M100-Ed32, published in 2022. The major changes in M100-Ed33 are listed below. Other minor or editorial changes were made to the general formatting and to some of the table footnotes and comments. Changes to the tables since the previous edition appear in boldface type. The following are additions or changes unless otherwise noted as "*Deleted.*"

M100 is updated and reviewed annually as new data and new agents become available. Use of outdated documents is strongly discouraged.

Section/Table	Changes
General	
Throughout	Revised text for testing and reporting to clarify relevant institutional stakeholders
CLSI Breakpoint Additions/Revisions Since 2010	**Revised to create 2 separate tables:** • CLSI Breakpoint Additions Since 2010 • CLSI Breakpoint Revisions Since 2010
CLSI Breakpoint Additions Since 2010	**Added:** • Plazomicin disk diffusion and MIC breakpoints for Enterobacterales (p. xxx)
CLSI Breakpoint Revisions Since 2010	**Revised:** • Amikacin – Disk diffusion and MIC breakpoints for Enterobacterales (p. xxxiii) – Disk diffusion and MIC breakpoints for *Pseudomonas aeruginosa* (p. xxxiv) • Gentamicin disk diffusion and MIC breakpoints for Enterobacterales (p. xxxiii) • Piperacillin disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv) • Piperacillin-tazobactam disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv) • Tobramycin – Disk diffusion and MIC breakpoints for Enterobacterales (p. xxxiv) – Disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv) ***Deleted:*** • Gentamicin disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv)

Overview of Changes (Continued)

Section/Table	Changes
General (Continued)	
CLSI Archived Resources	**Added:** • Former Tables 1A–1C regarding suggested groupings of antimicrobial agents approved by the US Food and Drug Administration for clinical use that should be considered for testing and reporting by microbiology laboratories, which have been replaced by new Tables 1A through 1P (p. xxxvii)
Instructions for Use of Tables	**Added:** • Test/Report Tiers and Additional Designations (pp. 3-5) • Selective and Cascade Reporting (pp. 6-7) **Revised:** • Introductory section to include new Tables 1A through 1P and to update test/report tiers and designations (p. 1) • Appropriate Agents for Routine Testing (p. 2) • Equivalent Agents (pp. 2-3) • Susceptible-dose dependent definition to include extended infusion in the dosage regimen information (p. 9) • Organisms Excluded from Table 2 to clarify *Aeromonas* spp. (p. 11)
Tables 2	**Added (where applicable):** • Urine-only (U) designation and associated footnote • Inv. designation for investigational agents • * designation for "Other" agents not included in Tables 1 ***Deleted:*** • Test/Report column
Tables 1. Antimicrobial Agents That Should Be Considered for Testing and Reporting by Microbiology Laboratories	
Introduction to Tables 1A-1P. Antimicrobial Agents That Should Be Considered for Testing and Reporting by Microbiology Laboratories (new)	**Added:** • Introductory text and warning box for Tables 1A-1P (p. 24)
Table 1A. Enterobacterales (not including inducible AmpC producers and *Salmonella/Shigella*) (new table)	**Added:** • Antimicrobial agents for Enterobacterales (not including inducible AmpC producers and *Salmonella/Shigella*) (pp. 26–27)
Table 1B. *Salmonella* and *Shigella* spp. (new table)	**Added:** • Antimicrobial agents for *Salmonella* and *Shigella* spp. (p. 28)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. Zone Diameter and/or MIC Breakpoints	
Table 2A. Zone Diameter and MIC Breakpoints for Enterobacterales	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 58) • Reference for comments regarding cephems and routine ESBL testing and cephems and third-generation cephalosporin resistance (p. 62) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 64) • Gentamicin, tobramycin, and amikacin combination therapy comment (p. 68) • Gentamicin, tobramycin, and amikacin dosage regimen comments (p. 68) • Plazomicin disk diffusion and MIC breakpoints and associated comments (p. 68) **Revised:** • General comment regarding testing fecal isolates of *Salmonella* and *Shigella* spp. (p. 58) • Comment regarding therapy for oral ampicillin (p. 60) • Comment regarding cephems and routine ESBL testing (p. 62) • Comment regarding cephems and third-generation cephalosporin resistance (p. 62) • Comment regarding carbapenems and elevated MICs (p. 66) • Gentamicin, tobramycin, and amikacin disk diffusion and MIC breakpoints (p. 68) • Gemifloxacin reporting comment (p. 69)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2B-1. Zone Diameter and MIC Breakpoints for *Pseudomonas aeruginosa*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 74) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 76) • Comment regarding combination therapy for tobramycin and amikacin (p. 78) • Tobramycin and amikacin dosage regimen comments (p. 78) **Revised:** • Piperacillin disk diffusion and MIC breakpoints and associated dosage regimen comment (p. 76) • Piperacillin-tazobactam disk diffusion and MIC breakpoints and associated dosage regimen comment (p. 76) • Tobramycin disk diffusion and MIC breakpoints (p. 78) • U designation for amikacin (p. 78) ***Deleted:*** • Gentamicin disk diffusion and MIC breakpoints
Table 2B-2. Zone Diameter and MIC Breakpoints for *Acinetobacter* spp.	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 80) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 81)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2B-3. Zone Diameter and MIC Breakpoints for *Burkholderia cepacia* complex	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 84) **Revised:** • Chloramphenicol reporting comment (p. 85)
Table 2B-4. Zone Diameter and MIC Breakpoints for *Stenotrophomonas maltophilia*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 86) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 87) • Levofloxacin ***Rx*** monotherapy comment (p. 87) **Revised:** • Chloramphenicol reporting comment (p. 87)
Table 2B-5. MIC Breakpoints for Other Non-Enterobacterales	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 90) **Revised:** • Comment regarding recommendations for testing and reporting *Aeromonas* spp. (p. 90) • Chloramphenicol reporting comment (p. 92)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2C. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 94) **Revised:** • Daptomycin reporting comment (p. 101) • Quinupristin-dalfopristin reporting comment (p. 102)
Table 2D. Zone Diameter and MIC Breakpoints for *Enterococcus* spp.	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 106) **Revised:** • Dalbavancin and daptomycin (*E. faecium* only) reporting comment (p. 109) • Erythromycin and fosfomycin reporting comments (p. 110) • Quinupristin-dalfopristin and tedizolid reporting comments (p. 111)
Table 2E. Zone Diameter and MIC Breakpoints for *Haemophilus influenzae* and *Haemophilus parainfluenzae*	**Added:** • MH-F agar as a medium for disk diffusion to the testing conditions box for *H. influenzae* (p. 112) • MH-F broth as a medium for broth dilution to the testing conditions box for *H. influenzae* (p. 112) • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 112) • General comment regarding the use of MH-F broth vs HTM broth in MIC testing (p. 113) • General comment regarding the use of MH-F agar broth vs HTM broth in disk diffusion testing (p. 113) **Revised:** • Routine QC recommendations box to clarify media for each QC strain (p. 112) • Ceftolozane-tazobactam reporting comment (p. 115)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2F. Zone Diameter and MIC Breakpoints for *Neisseria gonorrhoeae*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 118)
Table 2G. Zone Diameter and MIC Breakpoints for *Streptococcus pneumoniae*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 122) **Revised:** • Medium information for disk diffusion in testing conditions box (p. 122) • General comment regarding MIC testing of cefotaxime, ceftriaxone, meropenem, or penicillin reported with *S. pneumoniae* isolated from CSF (p. 123) • Comment regarding susceptibility to gemifloxacin, levofloxacin, and moxifloxacin (p. 127)
Table 2H-1. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. B-Hemolytic Group	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 130) **Revised:** • Dalbavancin and daptomycin reporting comments (p. 132) • Erythromycin, azithromycin, clarithromycin, and dirithromycin dosage regimen comment (p. 133) • Tedizolid reporting comment (p. 134)
Table 2H-2. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. Viridans Group	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 136) **Revised:** • Dalbavancin and daptomycin reporting comments (p. 138)
Table 2I. Zone Diameter and MIC Breakpoints for *Neisseria meningitidis*	**Revised:** • Chloramphenicol reporting comment (p. 142)

مجموعه جداول انتخاب شده از
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برای میکروارگانیسم های اولویت دار
در برنامه کشوری مهار مقاومت میکروبی
بر اساس راهنمای سازمان جهانی بهداشت
(GLASS)

ویرایش **هفتم**

سال ۱۴۰۲

کمیته تخصصی میکروب شناسی
آزمایشگاه مرجع سلامت
وزارت بهداشت، درمان و آموزش پزشکی

ویرایش هفتم این سند جایگزین ویرایش قبلی (ویرایش ششم - سال ۱۴۰۱) می باشد. تغییرات عمده در ویرایش هفتم این سند در جدول زیر فهرست شده است. تغییرات کوچک یا ویراستاری و توضیحات، با حروف پررنگ نوشته شده است.

Overview of Changes

Table	Changes
Escherichia coli	Added: • Levofloxacin disk diffusion breakpoints (page 6) Revised: • Gentamicin, and amikacin disk diffusion breakpoints (page 6)
Klebsiella pneumonia	Added: • Levofloxacin disk diffusion breakpoints (page 10) Revised: • Gentamicin, and amikacin disk diffusion breakpoints (page 9)
Salmonella spp.	Added: • Levofloxacin MIC breakpoints (page 12) • Imipenem, meropenem and tetracycline disk diffusion breakpoints (page 12)
Shigella spp.	Added: • Levofloxacin, imipenem, meropenem and tetracycline disk diffusion breakpoints (pages 13-14)
Tests for Extended-Spectrum β-Lactamases in *Escherichia coli, Klebsiella pneumonia, Salmonella* spp. *and Shigella* spp.	Added: • Note (page 15)
Pseudomonas aeruginosa	Revised: • Piperacillin-tazobactam and tobramycin disk diffusion breakpoints (pages 17-18) • Urine designation for amikacin (page 18) Deleted: • Gentamicin disk diffusion breakpoints
Acinetobacter spp.	Added: • Comment (d) (page 19)
Staphylococcus aureus	Added: • Levofloxacin disk diffusion breakpoints (page 23)
Enterococcus spp.	Added: • Levofloxacin disk diffusion breakpoints (page 25)

Suggested Groupings

از سال 2023 در مستند CLSI گروه بندی آنتی بیوتیک ها بر اساس گروههای A و B و C و O حذف شده و گروه بندی جدید تحت عنوان تی یر Tierجایگزین روش قدیمی شده است.

Table 1A. Enterobacterales (not including inducible AmpC producers and *Salmonella/Shigella*)[a]

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
Ampicillin			
Cefazolin	Cefuroxime		
Cefotaxime or ceftriaxone[b]	Cefepime[c]		
	Ertapenem Imipenem Meropenem	Cefiderocol	
		Ceftazidime-avibactam	
		Imipenem-relebactam	
		Meropenem-vaborbactam	
Amoxicillin-clavulanate Ampicillin-sulbactam			
Piperacillin-tazobactam			
Gentamicin	Tobramycin	Plazomicin	
	Amikacin		
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
	Cefotetan Cefoxitin		
	Tetracycline[d]		
			Aztreonam
			Ceftaroline[b]
			Ceftazidime[b]
			Ceftolozane-tazobactam
Urine Only			
Cefazolin (surrogate for uncomplicated UTI)[e]			
Nitrofurantoin			
		Fosfomycin[f] (*Escherichia coli*)	

Abbreviations: MDRO, multidrug-resistant organism; UTI, urinary tract infection.

Table 1A. Enterobacterales (Continued)

Footnotes

a. See Appendix B for species-specific intrinsic resistance profiles. If an antimicrobial agent-organism combination that is defined as intrinsically resistant is tested, the result hould be reported as resistant. Consideration may be given to adding comments regarding intrinsic resistance of agents not tested.

b. *Citrobacter freundii* complex, *Enterobacter cloacae* complex, *Hafnia alvei*, *Klebsiella* (formerly *Enterobacter) aerogenes*, *Morganella morganii*, *Providencia* spp., *Serratia marcescens*, and *Yersinia enterocolitica* may test susceptible to ceftriaxone, cefotaxime, ceftazidime, and ceftaroline, but these agents may be ineffective against these genera within a few days after initiation of therapy due to derepression of inducible AmpC β-lactamase. The risk of AmpC derepression during therapy is moderate to high with *C. freundii* complex, *E. cloacae complex*, and *K. aerogenes* and appears to be less frequent with *M. morganii*, *Providencia* spp., and *S. marcescens*.[1] Therefore, isolates that are initially susceptible may become resistant. Testing subsequent isolates may be warranted if clinically indicated.

c. Cefepime should be considered a Tier 1 agent for testing and/or reporting of *C. freundii* complex, *E. cloacae* complex, *H. alvei*, *K. aerogenes*, *M. morganii*, *Providencia* spp., *S. marcescens*, and *Y. enterocolitica* (see footnote b).[1]

d. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline or minocycline, or both.

e. See cefazolin comments in Table 2A for using cefazolin as a surrogate test for oral cephalosporins and for reporting cefazolin when used for therapy in uncomplicated UTIs.

f. Report only on *E. coli* isolated from the urinary tract.

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

Reference for Table 1A

[1] Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. IDSA Guidance on the treatment of antimicrobial-restant gram-negative infections: version 2.0. Infectious Diseases Society of America; 2022. Accessed 10 January 2023. https://www.idsociety.org/practice-guideline/amr-guidance-2.0/

Table 1B. *Salmonella* and *Shigella* spp.[a,b]

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
Ampicillin			
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
Cefotaxime or ceftriaxone			Ertapenem[c] Imipenem[c] Meropenem[c]
	Azithromycin[d]		
			Tetracycline[e]

Abbreviation: MDRO, multidrug-resistant organism.

Footnotes

a. Table 2A should be used for interpreting antimicrobial susceptibility testing results for *Salmonella* and *Shigella* spp.

b. WARNING: For *Salmonella* spp. and *Shigella* spp., aminoglycosides, first- and second-generation cephalosporins, and cephamycins may appear active *in vitro* but are not effective clinically and should not be reported as susceptible. Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources. However, susceptibility testing is indicated for all *Shigella* isolates. When fecal isolates of *Salmonella* and *Shigella* spp. are tested, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely. In addition, for extraintestinal isolates of *Salmonella* spp., a third-generation cephalosporin should be tested and reported. Azithromycin may be tested and reported per institutional guidelines.

c. Ertapenem, imipenem, and/or meropenem might be considered for testing and/or reporting for isolates resistant to all agents in Tiers 1 and 2, although there are limited clinical data suggesting their effectiveness for treating salmonellosis or shigellosis.[1]

d. Report only on *Salmonella enterica* ser. Typhi and *Shigella* spp.

e. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.

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

Reference for Table 1B

1 CDC Health Alert Network. Extensively drug-resistant *Salmonella* typhi infections among US residents without international travel. Accessed 10 January 2023. http://emergency.cdc.gov/han/2021/han00439.asp

Table 1C. *Pseudomonas aeruginosa*

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
Ceftazidime	**Imipenem**	**Cefiderocol**	
Cefepime	**Meropenem**	**Ceftazidime-avibactam**	
Piperacillin-tazobactam		**Ceftolozane-tazobactam**	
		Imipenem-relebactam	
Tobramycin			
Ciprofloxacin **Levofloxacin**			
			Aztreonam
Urine Only			
	Amikacin		

Abbreviation: MDRO, multidrug-resistant organism.

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

Table 1D. *Acinetobacter* spp.

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
Ampicillin-sulbactam			
Ceftazidime	**Imipenem**	**Cefiderocol**	
Cefepime	**Meropenem**		
Ciprofloxacin **Levofloxacin**			
Gentamicin **Tobramycin**	**Amikacin**		
	Piperacillin-tazobactam		
	Trimethoprim-sulfamethoxazole		
	Minocycline		**Doxycycline**
			Cefotaxime **Ceftriaxone**
			Colistin or polymyxin B
Urine only			
Tetracycline[a]			

Abbreviation: MDRO, multidrug-resistant organism.

Footnote

a. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.

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

Table 1H. *Staphylococcus* spp.

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
Azithromycin or clarithromycin or erythromycin[a]			
Clindamycin[a]			
Oxacillin[b,c,d,e] Cefoxitin[b,c,d] (surrogate for oxacillin)		Ceftaroline[f]	
Doxycycline Minocycline[a] Tetracycline[g]			
Trimethoprim-sulfamethoxazole			
Vancomycin[h]			
	Penicillin [b,i]		
	Daptomycin[h,j]		
	Linezolid	Tedizolid[f]	
		Rifampin[h,k]	
		Lefamulin[a,f]	
			Ciprofloxacin or levofloxacin Moxifloxacin
			Dalbavancin[f,h]
			Oritavancin[f,h]
			Telavancin[f,h]
			Gentamicin[l]
Urine Only			
Nitrofurantoin			

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

Table 1I. *Enterococcus* spp.

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
Ampicillin[a] Penicillin[b]			
	Vancomycin		
	Gentamicin[c] (high-level resistance testing only)	Streptomycin[c] (high-level resistance testing only)	
	Daptomycin[d,e]		
	Linezolid	Tedizolid	
			Dalbavancin[d,f]
			Oritavancin[d,f]
			Telavancin[d,f]
Urine only			
Nitrofurantoin			
	Ciprofloxacin Levofloxacin		
		Fosfomycin[g]	
		Tetracycline[h]	

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

Footnotes

a. The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. Ampicillin results may be used to predict susceptibility to amoxicillin-clavulanate, ampicillin-sulbactam, and piperacillin-tazobactam among non-β-lactamase-producing enterococci. Ampicillin susceptibility can be used to predict imipenem susceptibility, provided the species is confirmed to be *Enterococcus faecalis*.

b. Enterococci susceptible to penicillin are predictably susceptible to ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, and piperacillin-tazobactam for non-β-lactamase-producing enterococci. However, enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin. If penicillin results are needed, testing of penicillin is required. *Rx*: Combination therapy with high-dosage parenteral ampicillin, amoxicillin, penicillin, or vancomycin (for susceptible strains only) plus an aminoglycoside is usually indicated for serious enterococcal infections such as endocarditis, unless high-level resistance to both gentamicin and streptomycin is documented; such combinations are predicted to result in synergistic killing of enterococci.

c. See additional testing and reporting information in Table 3K.

Table 2A. Zone Diameter and MIC Breakpoints for Enterobacterales

Testing Conditions	
Medium:	Disk diffusion: MHA Broth dilution: CAMHB; iron-depleted CAMHB for cefiderocol (see Appendix I)[1] Agar dilution: MHA
Inoculum:	Broth culture method or colony suspension, equivalent to a 0.5 McFarland standard; positive blood culture broth for select antimicrobial agents with disk diffusion (see general comment [6]).
Incubation:	35°C ± 2°C; ambient air Disk diffusion: 16-18 hours Dilution methods: 16-20 hours

Routine QC Recommendations (see Tables 4A-1 and 5A-1 for acceptable QC ranges)

Escherichia coli ATCC®a 25922
Pseudomonas aeruginosa ATCC® 27853 (for carbapenems)
Staphylococcus aureus ATCC® 25923 (for disk diffusion) or *S. aureus* ATCC® 29213 (for dilution methods) when testing azithromycin against *Salmonella enterica* ser. Typhi *or Shigella* spp.
Refer to Tables 4A-2 and 5A-2 to select strains for routine QC of β-lactam combination agents.

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 Tables 3A, 3B, and 3C for additional testing, reporting, and QC for Enterobacterales.

General Comments

(1) Refer to Tables 1A-1B for antimicrobial agents that should be considered for testing and reporting by microbiology laboratories.

(2) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and no more than 6 disks on a 100-mm plate; disks should be placed no less than 24 mm apart, center to center (see M02,[2] Subchapter 3.6). Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement. 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*[3]). Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. Strains of *Proteus* spp. may swarm into areas of inhibited growth around certain antimicrobial agents. With *Proteus* spp., ignore the thin veil of swarming growth in an otherwise obvious zone of growth inhibition. 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.

(3) When fecal isolates of *Salmonella* and *Shigella* spp. are tested, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely. Data regarding whether amoxicillin should be used to treat shigellosis are conflicting. When reporting ampicillin results, state that treatment of shigellosis with amoxicillin might **have poorer efficacy compared with treatment with ampicillin.** In addition, for extraintestinal isolates of *Salmonella* spp., a third-generation cephalosporin should be tested and reported, and chloramphenicol may be tested and reported if requested. Susceptibility testing is indicated for typhoidal *Salmonella* (*S. enterica* ser. Typhi and *S. enterica* ser. Paratyphi A-C) isolated from extraintestinal and intestinal sources. Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources. In contrast, susceptibility testing is indicated for all *Shigella* isolates.

Table 2A. Enterobacterales (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	SDD	I	R	S	SDD	I	R	
AMINOGLYCOSIDES											
(46) **WARNING:** For *Salmonella* spp. and *Shigella* spp., aminoglycosides may appear active *in vitro* but are not effective clinically and should not be reported as susceptible.											
A	Gentamicin	10 µg	≥15	-	13-14^	≤12	≤4	-	8^	≥16	
A	Tobramycin	10 µg	≥15	-	13-14^	≤12	≤4	-	8^	≥16	
B	Amikacin	30 µg	≥17	-	15-16^	≤14	≤16	-	32^	≥64	
O	Kanamycin	30 µg	≥18	-	14-17^	≤13	≤16	-	32^	≥64	
O	Netilmicin	30 µg	≥15	-	13-14^	≤12	≤8	-	16^	≥32	
O	Streptomycin	10 µg	≥15	-	12-14^	≤11	-	-	-	-	
MACROLIDES											
B	Azithromycin	15 µg	≥13	-	-	≤12	≤16	-	-	≥32	(47) *S. enterica* ser. Typhi only: breakpoints are based on MIC distribution data and limited clinical data. (48) Breakpoints are based on a dosage regimen of 500 mg administered daily.
			≥16	-	11-15	≤10	≤8	-	16	≥32	(49) *Shigella* spp. only: azithromycin disk diffusion zones can be hazy and difficult to measure, especially *S. sonnei*. If an isolate has a zone of inhibition that is difficult to measure, an MIC method is recommended. Media source may affect the clarity of the end points for disk diffusion tests. See comment (48).
TETRACYCLINES											
(50) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.											
C	Tetracycline	30 µg	≥15	-	12-14	≤11	≤4	-	8	≥16	
O	Doxycycline	30 µg	≥14	-	11-13	≤10	≤4	-	8	≥16	
O	Minocycline	30 µg	≥16	-	13-15	≤12	≤4	-	8	≥16	

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
PENICILLINS										
Ampicillin	10 µg	≥ 17	-	14-16^	≤ 13	≤ 8	-	16^	≥ 32	**(7)** Results of ampicillin testing can be used to predict results for amoxicillin. **(8)** Breakpoints are based on an ampicillin dosage regimen of 2 g parenterally administered every 4-6 h or an amoxicillin dosage regimen of 1-2 g parenterally administered every 6 h. **(9)** Breakpoints when oral ampicillin is used **only** for therapy of **salmonellosis, shigellosis, or** uncomplicated UTIs due to *E. coli* **and** *P. mirabilis* are based on an ampicillin dosage regimen of 500 mg orally administered every 6 h or an amoxicillin dosage regimen of 250 mg orally administered every 8 h or 500 mg every 12 h. See general comment (3).
Piperacillin*		-	-	-	-	≤ 8	16	-	≥ 32	**(10)** Disk diffusion breakpoints have been removed because no disk correlate data are available for the revised piperacillin MIC breakpoints. Disk diffusion breakpoints will be reassessed if data become available.
Mecillinam*	10 µg	≥ 15	-	12-14^	≤ 11	≤ 8	-	16^	≥ 32	**(11)** For testing and reporting of *E. coli* urinary tract isolates only.

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
β-LACTAM COMBINATION AGENTS										
(12) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test SDD, intermediate, or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.										
Amoxicillin-clavulanate	20/10 µg	≥ 18	-	14-17^	≤ 13	≤8/4	-	16/8^	≥ 32/16	**(13)** Breakpoints are based on a dosage regimen of 1.2 g IV administered every 6 h. **(14)** Breakpoints when amoxicillin-clavulanate is used for therapy of uncomplicated UTIs or for completion of therapy for systemic infection are based on a dosage regimen of either 875/125 mg administered orally every 12 h or 500/125 mg every 8 h.
Ampicillin-sulbactam	10/10 µg	≥ 15	-	12-14^	≤ 11	≤ 8/4	-	16/8^	≥ 32/16	**(15)** Breakpoints are based on a dosage regimen of 3 g administered parenterally every 6 h.
Ceftolozane-tazobactam	30/10 µg	≥ 22	-	19-21^	≤ 18	≤ 2/4	-	4/4^	≥ 8/4	**(16)** Breakpoints are based on a dosage regimen of 3 g administered every 8 h for pneumonia and 1.5 g administered every 8 h for other indications.
Ceftazidime-avibactam	30/20 µg	≥ 21	-	-	≤ 20	≤ 8/4	-	-	≥ 16/4	**(17)** Breakpoints are based on a dosage regimen of 2.5 g every 8 h administered over 2 h. **(18)** Confirmatory MIC testing is indicated for isolates with zones of 20-22 mm to avoid reporting false-susceptible or false-resistant results.
Imipenem-relebactam	10/25 µg	≥ 25	-	21-24^	≤ 20	≤ 1/4	-	2/4^	≥ 4/4	**(19)** Breakpoints are based on a dosage regimen of 1.25 g administered every 6 h. **(20)** Breakpoints do not apply to the family Morganellaceae, which includes but is not limited to the genera *Morganella*, *Proteus*, and *Providencia*.

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
β-LACTAM COMBINATION AGENTS (Continued)										
Meropenem-vaborbactam	20/10 µg	≥ 18	-	15-17^	≤ 14	≤ 4/8	-	8/8^	≥ 16/8	**(21)** Breakpoints are based on a dosage regimen of 4 g every 8 h administered over 3 h.
Piperacillin-tazobactam	100/10 µg	≥ 25	21-24		≤ 20	≤ 8/4	16/4		≥ 32/4	**(22)** Breakpoints for susceptible are based on a dosage regimen of 3.375-4.5 g administered every 6 h as a 30-minute infusion. Breakpoints for SDD are based on a dosage regimen of 4.5 g administered every 6 h as a 3-h infusion or 4.5 g administered every 8 h as a 4-h infusion.
Ticarcillin-clavulanate*	75/10 µg	≥ 20	-	15-19^	≤ 14	≤ 16/2	-	32/2-64/2^	≥ 128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)										

(23) WARNING: For *Salmonella* spp. and *Shigella* spp., first- and second-generation cephalosporins and cephamycins may appear active *in vitro* but are not effective clinically and should not be reported as susceptible.

(24) Following evaluation of PK/PD properties, limited clinical data, and MIC distributions, revised breakpoints for cephalosporins (cefazolin, cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone) and aztreonam were first published in January 2010 (M100-S20) and are listed in this table. Cefuroxime (parenteral) was also evaluated; however, no change in breakpoints was necessary for the dosage indicated below. When using current breakpoints, routine ESBL testing is not necessary before reporting results. However, **in consultation with the antimicrobial stewardship team and other relevant institutional stakeholders, laboratories may decide to perform phenotypic or genotypic testing for ESBLs, and the results may be used to guide therapeutic management or** for epidemiological or infection prevention purposes. **Limitations of phenotypic and genotypic methods must be considered (see Table 3A introductory text).[4]**

Breakpoints for drugs with limited availability in many countries (eg, moxalactam, cefonicid, cefamandole, and cefoperazone) were not evaluated. If considering use of these drugs for *E. coli*, ***K. pneumoniae*** **and** ***K. oxytoca*****,** or *Proteus* spp., ESBL testing should be performed (see Table 3A). If isolates test ESBL positive, the results for moxalactam, cefonicid, cefamandole, and cefoperazone should be reported as resistant.

(25) Some Enterobacterales may develop resistance during therapy with third-generation cephalosporins as a result of derepression of AmpC β-lactamase. This derepression is most commonly seen with *Citrobacter freundii* complex, *Enterobacter cloacae* complex, and *Klebsiella* (formerly *Enterobacter*) *aerogenes*. Isolates that are initially susceptible may become resistant within **a few days** after initiation of therapy. Testing **subsequent** isolates may be warranted **if clinically indicated. The approach to reporting AST results for these organisms should be determined in consultation with the antimicrobial stewardship team and other relevant institutional stakeholders. See Table 1A, footnotes b and c.[4]**

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)										
Cefazolin	30 µg	≥23	-	20-22	≤19	≤2	-	4	≥8	**(26)** Breakpoints when cefazolin is used for therapy of infections other than uncomplicated UTIs due to *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Breakpoints are based on a dosage regimen of 2 g administered every 8 h. See comment (24).
Cefazolin **(U)**[b]	30 µg	≥15	-	-	≤14	≤16	-	-	≥32	**(27)** Breakpoints when cefazolin is used for therapy of uncomplicated UTIs due to *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Breakpoints are based on a dosage regimen of 1 g administered every 12 h. See additional information in CEPHEMS (ORAL).
Ceftaroline	30 µg	≥23	-	20-22^	≤19	≤0.5	-	1^	≥2	**(28)** Breakpoints are based on a dosage regimen of 600 mg administered every 12 h.
Cefepime	30 µg	≥25	19-24	-	≤18	≤2	4-8	-	≥16	**(29)** The breakpoint for susceptible is based on a dosage regimen of 1 g administered every 12 h. The breakpoint for SDD is based on dosage regimens that result in higher cefepime exposure, either higher doses or more frequent doses or both, up to approved maximum dosage regimens. See Appendix E for more information about breakpoints and dosage regimens. Also see the definition of SDD in the Instructions for Use of Tables section.
Cefotaxime or ceftriaxone	30 µg 30 µg	≥26 ≥23	-	23-25^ 20-22^	≤22 ≤19	≤1 ≤1	-	2^ 2^	≥4 ≥4	**(30)** Breakpoints are based on a dosage regimen of 1 g administered every 24 h for ceftriaxone and 1 g administered every 8 h for cefotaxime. See comment (24).

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)										
Cefotetan	30 µg	≥ 16	-	13-15^	≤ 12	≤ 16	-	32^	≥ 64	
Cefoxitin	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	(31) Breakpoints are based on a dosage regimen of at least 8 g per day (eg, 2 g administered every 6 h).
Cefuroxime (parenteral)	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	(32) Breakpoints are based on a dosage regimen of 1.5 g administered every 8 h. See comment (24).
Ceftazidime	30 µg	≥ 21	-	18-20^	≤ 17	≤ 4	-	8^	≥ 16	(33) Breakpoints are based on a dosage regimen of 1 g administered every 8 h. See comment (24).
Cefamandole•	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	See comment (24).
Cefmetazole•	30 µg	≥ 16	-	13-15^	≤ 12	≤ 16	-	32^	≥ 64	(34) Insufficient new data exist to reevaluate breakpoints listed here.
Cefonicid•	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	See comment (24).
Cefoperazone•	75 µg	≥ 21	-	16-20	≤ 15	≤ 16	-	32	≥ 64	See comment (24).
Ceftizoxime•	30 µg	≥ 25	-	22-24^	≤ 21	≤ 1	-	2^	≥ 4	(35) Breakpoints are based on a dosage regimen of 1 g administered every 12 h. See comment (24).
Moxalactam•	30 µg	≥ 23	-	15-22^	≤ 14	≤ 8	-	16-32^	≥ 64	See comment (24).
Cefiderocol	30 µg	≥ 16	-	9-15^	≤ 8	≤ 4	-	8^	≥ 16	(36) Breakpoints are based on a dosage regimen of 2 g every 8 h administered over 3 h. **(37) The accuracy and reproducibility of cefiderocol testing results by disk diffusion and broth microdilution are markedly affected by iron concentration and inoculum preparation and may vary by disk and media manufacturer. Depending on the type of variance observed, false-resistant or false-susceptible results may occur. Testing subsequent isolates is encouraged. Discussion with prescribers and antimicrobial stewardship members regarding the potential for inaccuracies is recommended.**

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
CEPHEMS (ORAL)										
Cefuroxime (oral)	30 µg	≥23	-	15–22^	≤14	≤4		8–16^	≥32	See comment (38).
Cefazolin **(U)**[b] (surrogate test for oral cephalosporins and uncomplicated UTIs)	30 µg	≥15	-	-	≤14	≤16	-	-	≥32	**(38)** Breakpoints are for cefazolin when used as a surrogate test to predict results for the oral agents cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, cephalexin, and loracarbef when used for therapy of uncomplicated UTIs due to *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Cefazolin tested as a surrogate may overcall resistance to cefdinir, cefpodoxime, and cefuroxime. If cefazolin tests resistant, test these drugs individually if needed for therapy.
Loracarbef*	30 µg	≥18	-	15–17^	≤14	≤8	-	16^	≥32	**(39)** Do not test *Citrobacter*, *Providencia*, or *Enterobacter* spp. with cefdinir or loracarbef by disk diffusion because false-susceptible results have been reported. See comment (38).
Cefaclor*	30 µg	≥18	-	15–17^	≤14	≤8	-	16^	≥32	See comment (38).
Cefdinir*	5 µg	≥20	-	17–19^	≤16	≤1	-	2^	≥4	See comments (38) and (39).
Cefixime*	5 µg	≥19	-	16–18^	≤15	≤1	-	2^	≥4	**(40)** Do not test *Morganella* spp. with cefixime, cefpodoxime, or cefetamet by disk diffusion.
Cefpodoxime*	10 µg	≥21	-	18–20^	≤17	≤2	-	4^	≥8	See comments (38) and (40).
Cefprozil*	30 µg	≥18	-	15–17^	≤14	≤8	-	16^	≥32	**(41)** Do not test *Providencia* spp. with cefprozil by disk diffusion because false-susceptible results have been reported. See comment (38).
Cefetamet **(Inv.)**	10 µg	≥18	-	15–17^	≤14	≤4	-	8^	≥16	See comment (40).
Ceftibuten **(U, Inv.)**[b]	30 µg	≥21	-	18–20^	≤17	≤8	-	16^	≥32	

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
MONOBACTAMS										
Aztreonam	30 µg	≥ 21	-	18-20^	≤ 17	≤4	-	8^	≥ 16	**(42)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h. See comment (24).
CARBAPENEMS										
(43) Following evaluation of PK/PD properties, limited clinical data, and MIC distributions that include recently described carbapenemase-producing strains, revised breakpoints for carbapenems were first published in June 2010 (M100-S20-U) and are listed below. Because of limited treatment options for infections caused by organisms with carbapenem MICs or zone diameters in the intermediate range, clinicians may wish to design carbapenem dosage regimens that use maximum recommended doses and possibly prolonged intravenous infusion regimens, as has been reported in the literature.[5-8] Consultation with an infectious diseases **specialist** is recommended for isolates for which the carbapenem MICs or zone diameter results from disk diffusion testing are in the intermediate or resistant ranges. **Institutional treatment guidelines, infection prevention procedures, or epidemiological investigations may necessitate identification of carbapenemase-producing Enterobacterales. Isolates with elevated carbapenem MICs (intermediate or resistant) can be tested for carbapenemase production by a phenotypic and/or a molecular assay (refer to Tables 3B and 3C for methods). See Appendix H, Table H3 regarding suggestions for reporting when mechanism of resistance-based testing (molecular and phenotypic methods) is discordant with phenotypic AST.** The following information is provided as background on carbapenemases in Enterobacterales that are largely responsible for MICs and zone diameters in the intermediate and resistant ranges, and thus the rationale for setting revised carbapenem breakpoints: • The clinical effectiveness of carbapenem treatment of infections produced by isolates for which the carbapenem MIC or disk diffusion test results are within the intermediate range is uncertain due to lack of controlled clinical studies. Imipenem MICs for *Proteus* spp., *Providencia* spp., and *Morganella morganii* tend to be higher (eg, MICs in the intermediate or resistant range) than meropenem or doripenem MICs. These isolates may have elevated imipenem MICs by mechanisms other than production of carbapenemases.									
Doripenem*	10 µg	≥ 23	-	20-22^	≤ 19	≤1	-	2^	≥ 4	**(44)** Breakpoints are based on a dosage regimen of 500 mg administered every 8 h.
Ertapenem	10 µg	≥ 22	-	19-21^	≤ 18	≤0.5	-	1^	≥ 2	**(45)** Breakpoints are based on a dosage regimen of 1 g administered every 24 h.
Imipenem	10 µg	≥ 23	-	20-22^	≤ 19	≤1	-	2^	≥ 4	**(46)** Breakpoints are based on a dosage regimen of 500 mg administered every 6 h or 1 g every 8 h.
Meropenem	10 µg	≥ 23	-	20-22^	≤ 19	≤1	-	2^	≥ 4	**(47)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h.

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
LIPOPEPTIDES										
(48) WARNING: Clinical and PK/PD data demonstrate colistin and polymyxin B have limited clinical efficacy, even if an intermediate result is obtained. Alternative agents are strongly preferred. Colistin and polymyxin B should be used in combination with one or more active antimicrobial agents. Consultation with an infectious diseases specialist is recommended. **(49)** Several species are intrinsically resistant to the lipopeptides (colistin and polymyxin B). Refer to Appendix B.										
Colistin or polymyxin B•		-	-	-	-	-	-	≤ 2	≥ 4	**(50)** Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses (see International Consensus Guidelines[9]). **(51)** Polymyxin B should be given with a loading dose and maximum recommended doses (see International Consensus Guidelines[9]). **(52)** When colistin or polymyxin B is given systemically, neither is likely to be effective for pneumonia. **(53)** For colistin, broth microdilution, CBDE, and CAT MIC methods are acceptable. For polymyxin B, broth microdilution is the only approved method. Disk diffusion and gradient diffusion methods should not be performed (see Table 3D).
		-	-	-	-	-	-	≤ 2	≥ 4	

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
AMINOGLYCOSIDES										
(54) **WARNING:** For *Salmonella* spp. and *Shigella* spp., aminoglycosides may appear active *in vitro* but are not effective clinically and should not be reported as susceptible. **(55) Breakpoints for gentamicin, tobramycin, and amikacin are based on population distributions of various species, PK/PD target attainment analyses with an end point of net bacterial stasis and limited clinical data. Clinical outcomes data for aminoglycosides as monotherapy for systemic infections are limited and have resulted in worse treatment outcomes (for infections outside of the urinary tract) compared with other therapies. Combination therapy for most indications other than UTIs should be considered. Consultation with an infectious diseases specialist is recommended.**										
Gentamicin	10 µg	**≥ 18**	-	**15-17^**	**≤ 14**	**≤ 2**	-	**4^**	**≥ 8**	**(56) Breakpoints are based on a dosage regimen of 7 mg/kg parenterally administered every 24 h.**
Tobramycin	10 µg	**≥ 17**	-	13-**16^**	≤ 12	**≤ 2**	-	**4^**	**≥ 8**	**(57) Breakpoints are based on a dosage regimen of 7 mg/kg parenterally administered every 24 h.**
Amikacin	30 µg	**≥ 20**	-	**17-19^**	**≤ 16**	**≤ 4**	-	**8^**	**≥ 16**	**(58) Breakpoints are based on a dosage regimen of 15 mg/kg parenterally administered every 24 h.**
Plazomicin	**30 µg**	**≥ 18**	-	**15-17^**	**≤ 14**	**≤ 2**	-	**4^**	**≥ 8**	**(59) Breakpoints are based on a dosage regimen of 15 mg/kg every 24 h over 30 minutes.** **See comment (20).**
Kanamycin*	30 µg	≥ 18	-	14-17^	≤ 13	≤ 16	-	32^	≥ 64	
Netilmicin*	30 µg	≥ 15	-	13-14^	≤ 12	≤ 8	-	16^	≥ 32	
Streptomycin*	10 µg	≥ 15	-	12-14^	≤ 11	-	-	-	-	
MACROLIDES										
Azithromycin	15 µg	≥ 13	-	-	≤ 12	≤ 16	-	-	≥ 32	**(60)** *S. enterica* ser. Typhi only: breakpoints are based on MIC distribution data and limited clinical data. **(61)** Breakpoints are based on a dosage regimen of 500 mg administered daily.
		≥ 16	-	11-15	≤ 10	≤ 8	-	16	≥ 32	**(62)** *Shigella* spp. only: azithromycin disk diffusion zones can be hazy and difficult to measure, especially *S. sonnei*. If an isolate has a zone of inhibition that is difficult to measure, an MIC method is recommended. Media source may affect the clarity of the end points for disk diffusion tests. See comment (61).

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
TETRACYCLINES										
(63) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.										
Tetracycline	30 µg	≥ 15	-	12-14	≤ 11	≤ 4	-	8	≥ 16	
Doxycycline*	30 µg	≥ 14	-	11-13	≤ 10	≤ 4	-	8	≥ 16	
Minocycline*	30 µg	≥ 16	-	13-15	≤ 12	≤ 4	-	8	≥ 16	
QUINOLONES AND FLUOROQUINOLONES for Enterobacterales except *Salmonella* spp. (Please refer to Glossary I.)										
Ciprofloxacin	5 µg	≥ 26	-	22-25^	≤ 21	≤ 0.25	-	0.5^	≥ 1	**(64)** Breakpoints for ciprofloxacin are based on a dosage regimen of 400 mg IV or 500 mg orally administered every 12 h. **(65)** Breakpoints for levofloxacin are based on a dosage regimen of 750 mg administered every 24 h.
Levofloxacin	5 µg	≥ 21		17-20^	≤ 16	≤ 0.5	-	1^	≥ 2	
Cinoxacin* **(U)**[b]	100 µg	≥ 19	-	15-18^	≤ 14	≤ 16	-	32^	≥ 64	
Enoxacin* **(U)**[b]	10 µg	≥ 18	-	15-17^	≤ 14	≤ 2	-	4^	≥ 8	
Gatifloxacin*	5 µg	≥ 18	-	15-17^	≤ 14	≤ 2	-	4^	≥ 8	
Gemifloxacin*	5 µg	≥ 20	-	16-19	≤ 15	≤ 0.25	-	0.5	≥ 1	**(66) Report only on** *K. pneumoniae*.
Grepafloxacin*	5 µg	≥ 18	-	15-17	≤ 14	≤ 1	-	2	≥ 4	
Lomefloxacin*	10 µg	≥ 22	-	19-21^	≤ 18	≤ 2	-	4^	≥ 8	
Nalidixic acid* **(U)**[b]	30 µg	≥ 19	-	14-18	≤ 13	≤ 16	-	-	≥ 32	
Norfloxacin* **(U)**[b]	10 µg	≥ 17	-	13-16	≤ 12	≤ 4	-	8	≥ 16	
Ofloxacin*	5 µg	≥ 16	-	13-15^	≤ 12	≤ 2	-	4^	≥ 8	
Fleroxacin **(Inv.)**	5 µg	≥ 19	-	16-18^	≤ 15	≤ 2	-	4^	≥ 8	

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
QUINOLONES AND FLUOROQUINOLONES for *Salmonella* spp. (Please refer to Glossary I.)										
(67) For testing and reporting of *Salmonella* spp. (including *S. enterica* ser. Typhi and *S. enterica* ser. Paratyphi A-C). Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources. **(68)** The preferred test for assessing fluoroquinolone susceptibility or resistance in *Salmonella* spp. is a ciprofloxacin MIC test. A levofloxacin or ofloxacin MIC test can be performed if either agent, respectively, is the fluoroquinolone of choice in a specific facility. If a ciprofloxacin, levofloxacin, or ofloxacin MIC or ciprofloxacin disk diffusion test cannot be done, pefloxacin disk diffusion may be used as surrogate test to predict ciprofloxacin susceptibility. **(69)** No single test detects resistance resulting from all possible fluoroquinolone resistance mechanisms that have been identified in *Salmonella* spp.										
Ciprofloxacin	5 µg	≥ 31	-	21-30^	≤ 20	≤ 0.06	-	0.12-0.5 ^	≥ 1	**(70)** Isolates of *Salmonella* spp. that test not susceptible to ciprofloxacin, levofloxacin, ofloxacin, or pefloxacin may be associated with clinical failure or delayed response in fluoroquinolone-treated patients with salmonellosis.
Levofloxacin	-	-	-	-	-	≤ 0.12	-	0.25-1^	≥ 2	
Ofloxacin	-	-	-	-	-	≤ 0.12	-	0.25-1^	≥ 2	
Pefloxacin **(Inv.)** (surrogate test for ciprofloxacin)	5 µg	≥ 24	-	-	≤ 23	-	-	-	-	**(71)** Report results as ciprofloxacin susceptible or resistant based on the pefloxacin test result. Pefloxacin will not detect resistance in *Salmonella* spp. due to *aac(6')-Ib-cr*. Pefloxacin disks are not available in the United States. See comment (69).
FOLATE PATHWAY ANTAGONISTS										
Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥ 16	-	11-15	≤ 10	≤ 2/38	-	-	≥ 4/76	See general comment (3).
Sulfonamides• **(U)**[b]	250 or 300 µg	≥ 17	-	13-16	≤ 12	≤ 256	-	-	≥ 512	**(72)** Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations.
Trimethoprim• **(U)**[b]	5 µg	≥ 16	-	11-15	≤ 10	≤ 8	-	-	≥ 16	
PHENICOLS										
Chloramphenicol•	30 µg	≥ 18	-	13-17	≤ 12	≤ 8	-	16	≥ 32	**(73)** Not routinely reported on isolates from the urinary tract.

Table 2A. Enterobacterales (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
FOSFOMYCINS										
Fosfomycin **(U)**[b]	200 µg	≥16	-	13-15	≤12	≤64	-	128	≥256	**(74)** Disk diffusion and MIC breakpoints apply only to *E. coli* urinary tract isolates and should not be extrapolated to other species of Enterobacterales. **(75)** The 200-µg fosfomycin disk contains 50 µg glucose-6-phosphate. **(76)** The only approved MIC method for testing is agar dilution using agar media supplemented with 25 µg/mL of glucose-6-phosphate. Broth dilution MIC testing should not be performed.
NITROFURANS										
Nitrofurantoin **(U)**[b]	300 µg	≥17	-	15-16	≤14	≤32	-	64	≥128	

Abbreviations: **AST, antimicrobial susceptibility testing;** ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CAT, colistin agar test; CBDE, colistin broth disk elution; eCIM, EDTA-modified carbapenem inactivation method; ESBL, extended-spectrum β-lactamase; I, intermediate; **Inv., investigational agent;** IV, intravenous; mCIM, modified carbapenem inactivation method; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; PK/PD, pharmacokinetic/pharmacodynamic; QC, quality control; R, resistant; S, susceptible; SDD, susceptible-dose dependent; **U, urine;** UTI, urinary tract infection.
Symbols: ^, designation for agents that have the potential to concentrate in the urine; ***, designation for "Other" agents that are not included in Tables 1 but have established clinical breakpoints.**

Footnotes

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

b. Report only on organisms isolated from the urinary tract.

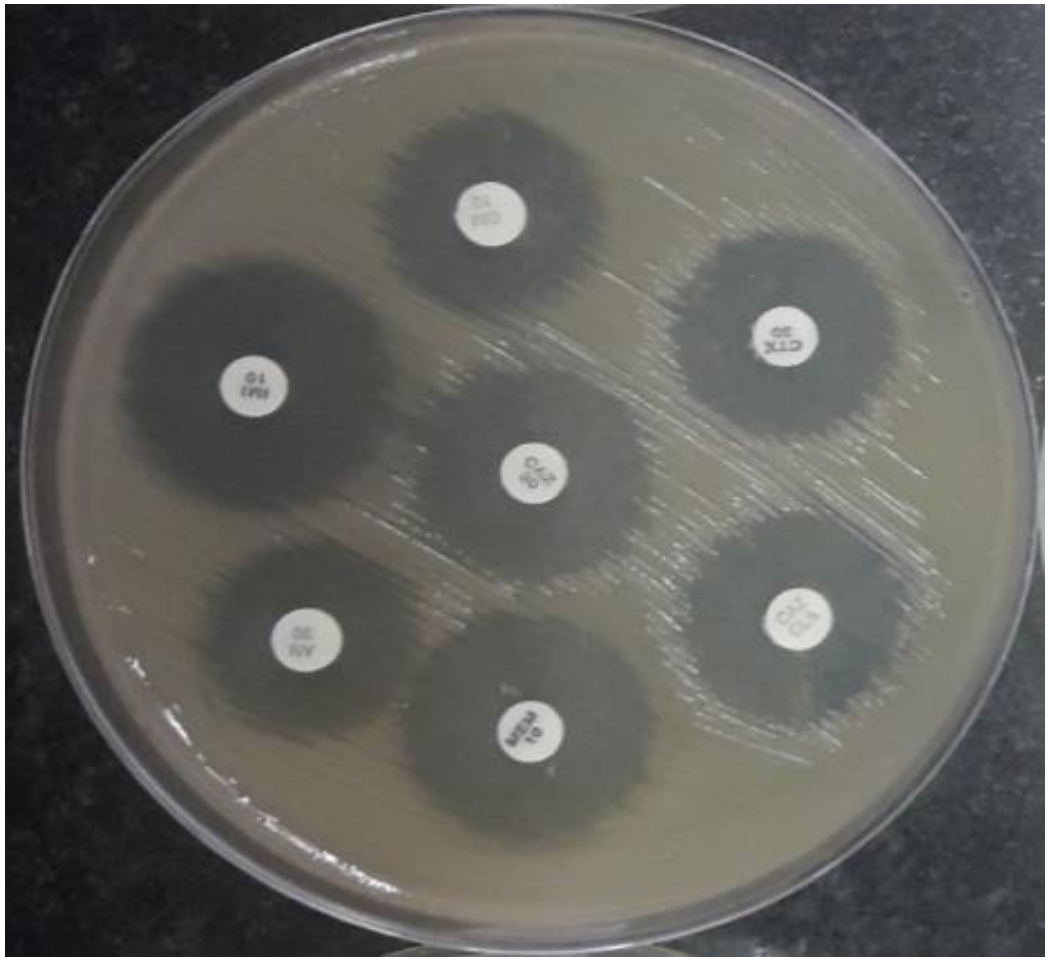
آنالیز نتایج آنتی بیوگرام باکتری M2

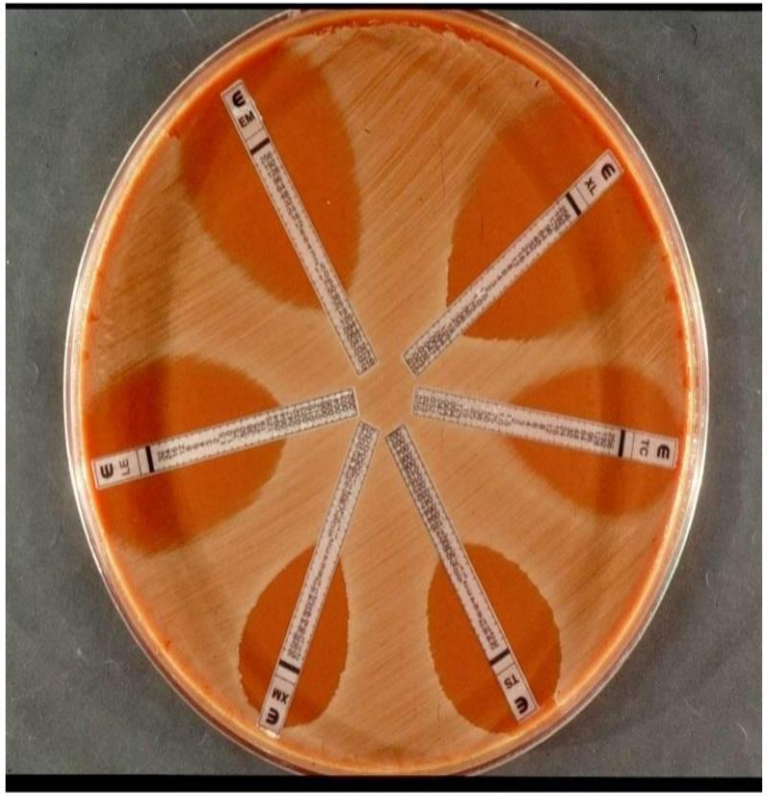
نام دیسک	تعداد استفاده	درصد استفاده	نتایج	تعداد گزارش	درصد گزارش
Azithromycin	80	%0.67	R I S	5 2 73	%6.25 %2.50 %91.25
Cephalothin	76	%0.64	R I S	74 1 1	%97.37 %1.32 %1.32
Cephalexin	89	%0.74	R I S	84 1 4	%94.38 %1.12 %4.49
Clindamycin	14	%0.12	S R	1 13	%7.14 %92.86
Erythromycin	15	%0.13	R I	12 3	%80.00 %20.00
Penicillin	24	%0.20	S R	4 20	%16.67 %83.33
Vancomycin	12	%0.10	I R	2 10	%16.67 %83.33
Vancomycin MIC E test	6	%0.05	R	6	%100.00

نام دیسک	تعداد استفاده	درصد استفاده	نتایج	نتیجه صحیح	تعداد گزارش	درصد گزارش
Amikacin	755	%6.31	I R S	I CLSI Group: O	260 235 255 5	%34.44 %31.13 %33.77 %0.66
Cefazolin	431	%3.60	R I S	R CLSI Group: U	2 416 6 7	%0.46 %96.52 %1.39 %1.62
Cefepime	197	%1.65	R I S	R CLSI Group: O	1 179 9 8	%0.51 %90.86 %4.57 %4.06
Cefixime	495	%4.14	R I S	R CLSI Group: O	468 8 16 3	%94.55 %1.62 %3.23 %0.61
Cefotaxime	401	%3.35	R I S	R CLSI Group: O	378 7 16	%94.26 %1.75 %3.99
Ceftazidime	376	%3.14	I S R	R CLSI Group: O	18 20 5 333	%4.79 %5.32 %1.33 %88.56
Ceftizoxime	119	%0.99	I S R	R CLSI Group: O	21 14 84	%17.65 %11.76 %70.59
Ceftriaxone	611	%5.11	R I S	R CLSI Group: O	584 8 17 2	%95.58 %1.31 %2.78 %0.33

نام دیسک	تعداد استفاده	درصد استفاده	نتایج	نتیجه صحیح	تعداد گزارش	درصد گزارش
Ciprofloxacin	1341	%11.21	I S R	R CLSI Group: O	7 46 5 1283	%0.52 %3.43 %0.37 %95.67
Imipenem	439	%3.67	I S R	S CLSI Group: O	78 236 4 121	%17.77 %53.76 %0.91 %27.56
Levofloxacin	137	%1.15	R S	R CLSI Group: O	132 5	%96.35 %3.65
Meropenem	163	%1.36	I S R	S CLSI Group: O	1 25 103 34	%0.61 %15.34 %63.19 %20.86
Nalidixic acid	521	%4.36	R I S	R CLSI Group: U	5 497 6 13	%0.96 %95.39 %1.15 %2.50
Nitrofurantoin	1496	%12.51	I S R	S CLSI Group: U	46 1420 2 28	%3.07 %94.92 %0.13 %1.87
Norfloxacin	153	%1.28	I S R	R CLSI Group: U	1 9 3 140	%0.65 %5.88 %1.96 %91.50
Ofloxacin	102	%0.85	R S	R CLSI Group: O	98 1 3	%96.08 %0.98 %2.94
Tetracycline	161	%1.35	I R S	S CLSI Group: O	11 6 144	%6.83 %3.73 %89.44
Trimethoprim-sulfamethoxazole	1302	%10.89	R S I	S CLSI Group: O	4 11 1276 11	%0.31 %0.84 %98.00 %0.84

Anti susceptibility testing



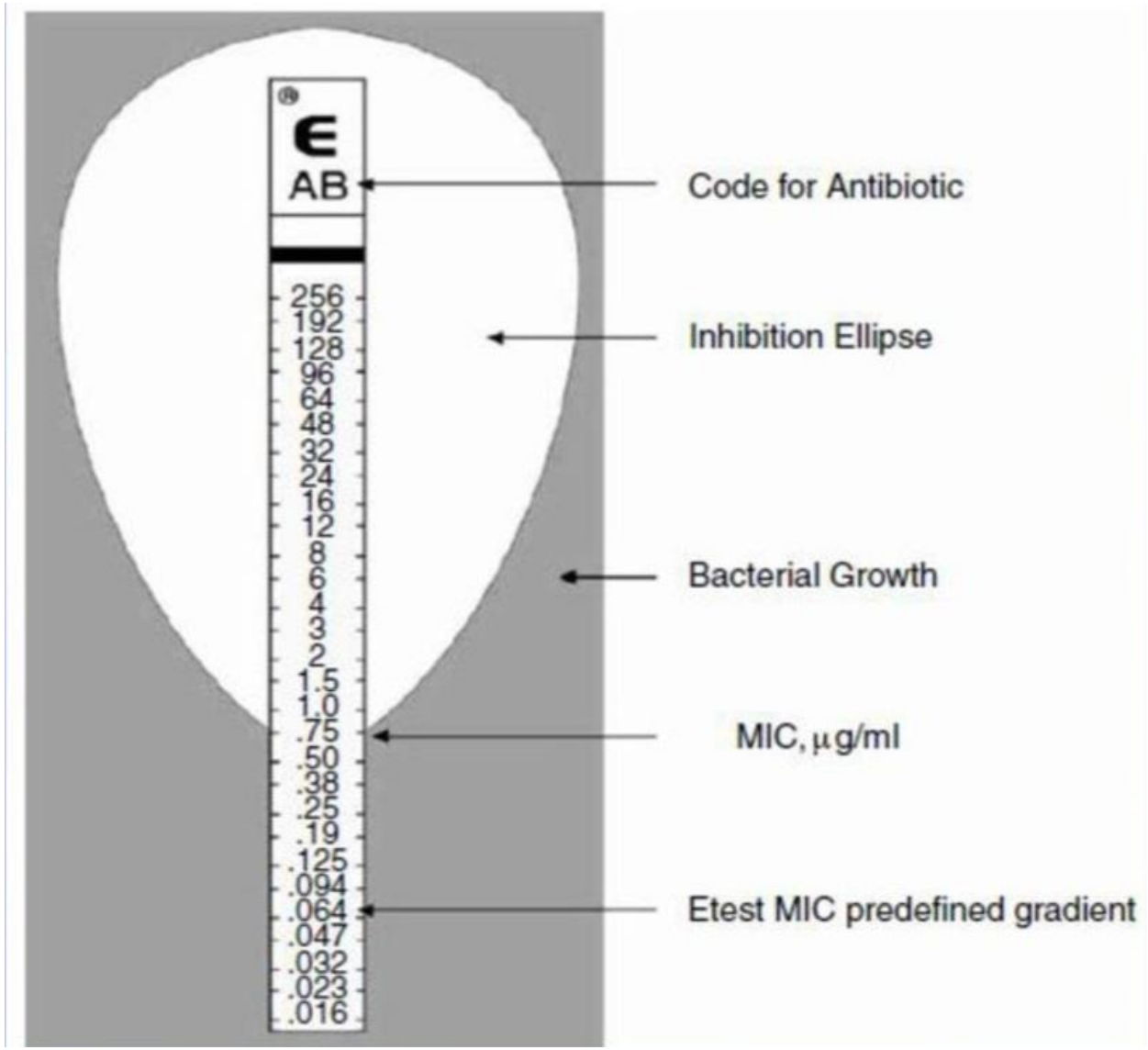


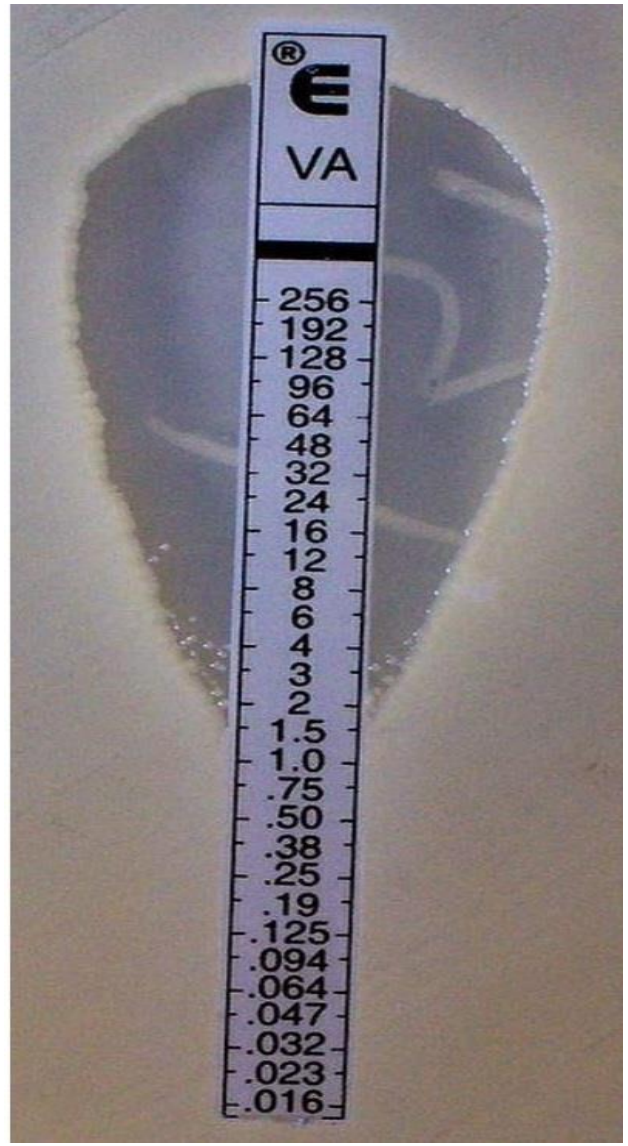
روش های متداول تعیین حساسیت آنتی بیوتیکی

دیسک دیفیوژن (کربی بائر)

براث میکرودایلوشن MIC

E –test


AB
256
192
128
96
64
48
32
24
16
12
8
6
4
3
2
1.5
1.0
.75
.50
.38
.25
.19
.125
.094
.064
.047
.032
.023
.016
Code for Antibiotic
Inhibition Ellipse
Bacterial Growth
MIC, μg/ml
Etest MIC predefined gradient


VA
256
192
128
96
64
48
32
24
16
12
8
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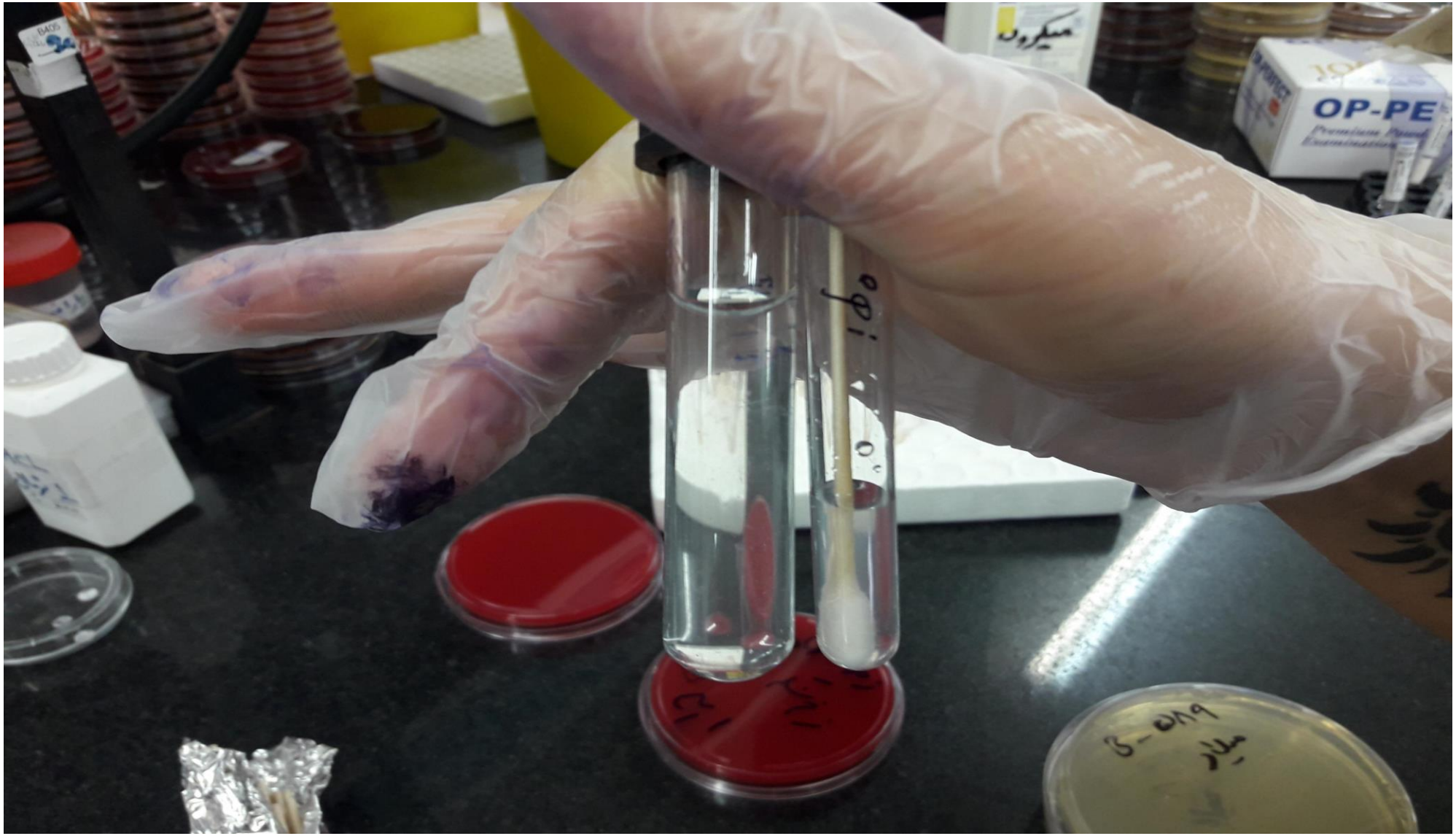
4
3
2
1.5
1.0
.75
.50
.38
.25
.19
.125
.094
.064
.047
.032
.023
.016

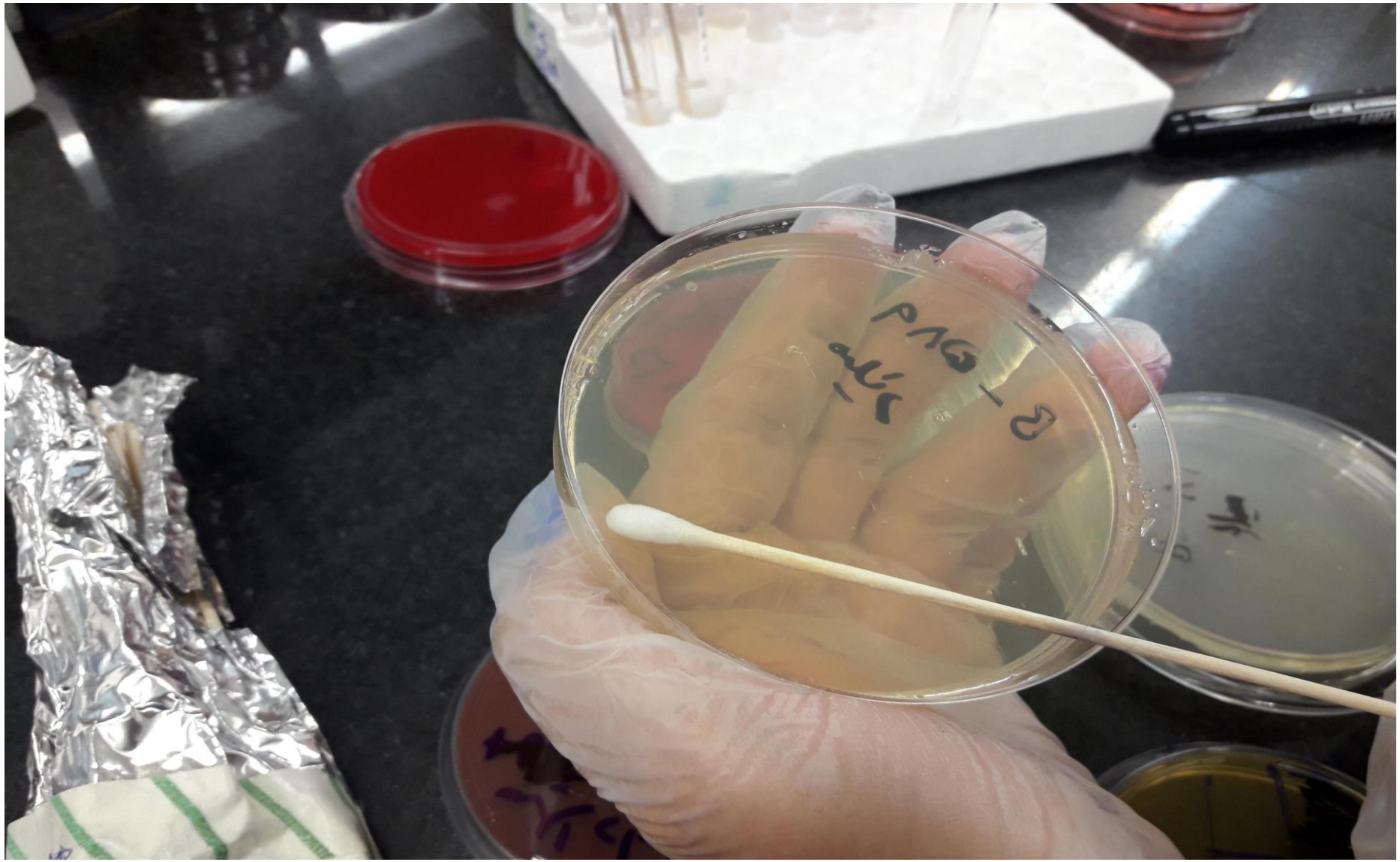
Disk diffusion method

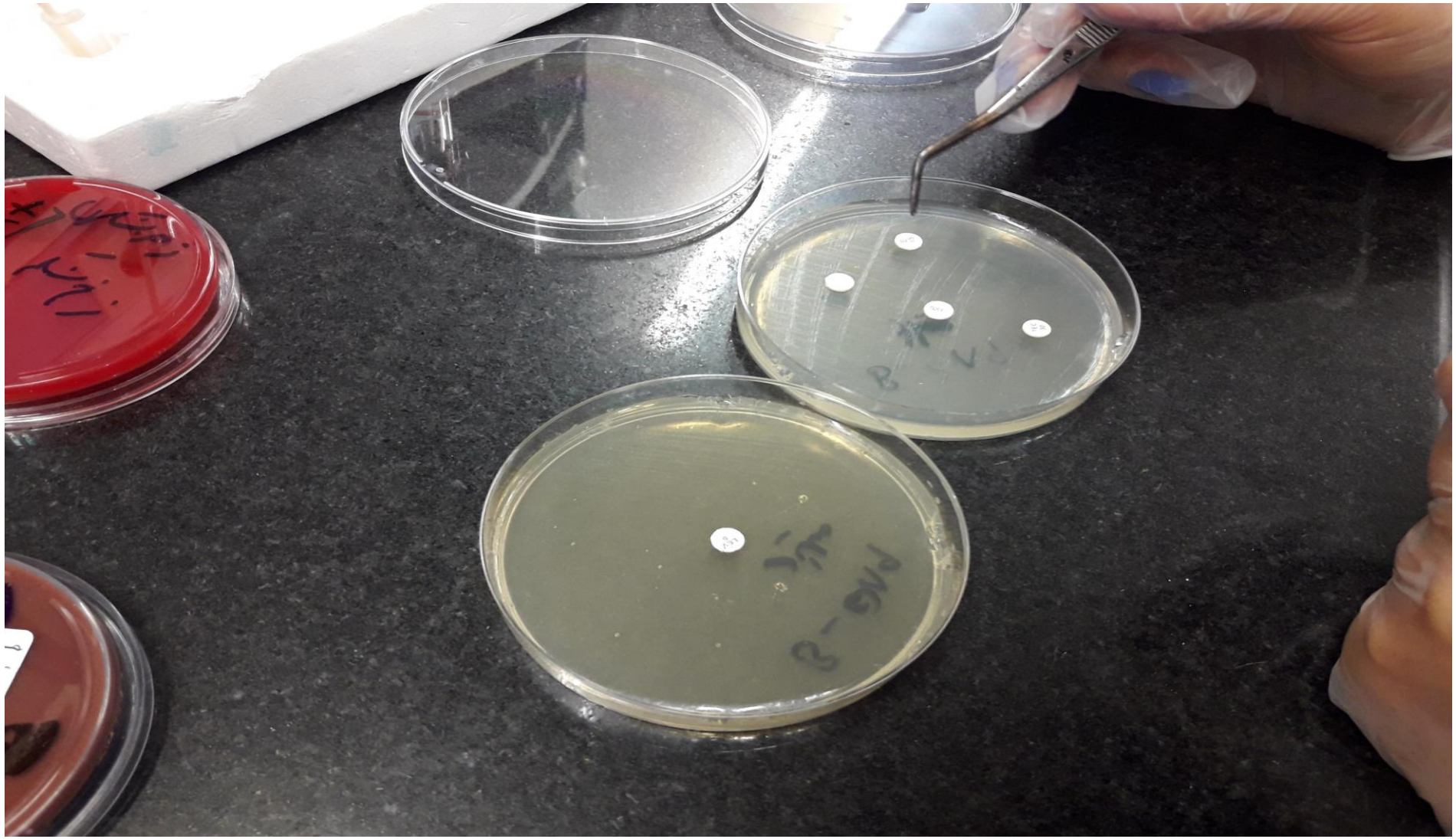
- ❖ استفاده از محیط های کشت ، مواد مصرفی و دیسک های آنتی بیوتیک کنترل کیفی شده
- ❖ تهیه اسمیر جهت رنگ آمیزی گرم و مشاهده میکروسکوپی
- ❖ استفاده از کلنی های کشت تازه و خالص باکتری
- ❖ تهیه سوسپانسیون میکروبی
- ❖ استفاده از استاندارد نیم مک فارلند
- ❖رعایت فواصل زمانی مراحل انجام تست (۱۵- ۱۵ -۱۵)

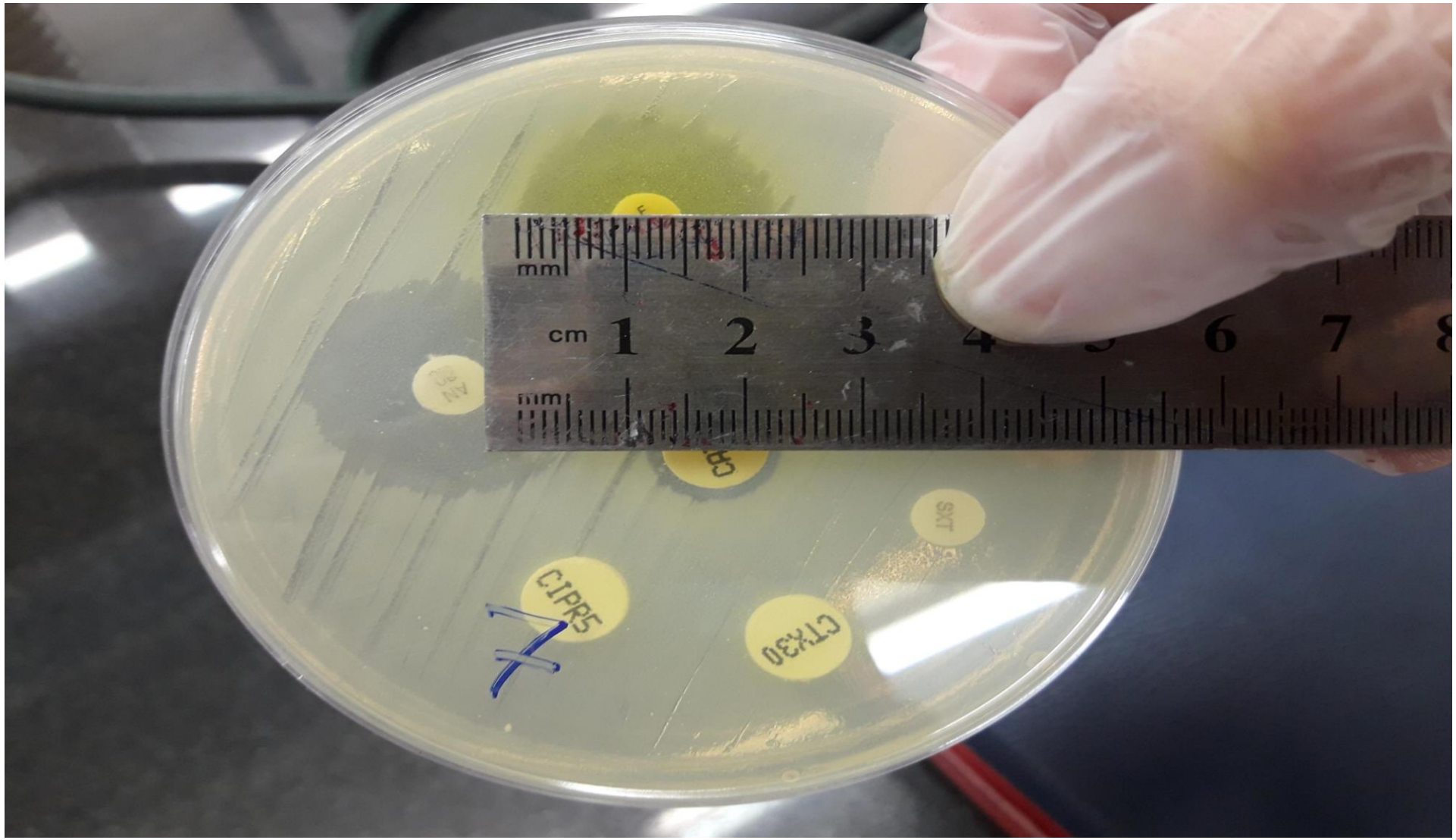
- دمای ذخیره سازی دیسک های آنتی بیوتیک حتما طبق توصیه کمپانی سازنده صورت گیرد .(درب یخچال،کارباپنم ها)
- انتخاب دیسک های آنتی بیوتیک حتما بر اساس نوع باکتری ، محل و منشا جداسازی باکتری و بر اساس جدول استاندارد CLSI باید صورت گیرد .
- برای مراکز درمانی بیمارستانی بهتر است پنل آنتی بیوتیک های هر گروه از باکتریها به اصطلاح بومی سازی شود. یعنی تلفیقی از آنتی بیوتیک های منتخب جدول CLSI و آنچه پزشکان و تیم کنترل عفونت بیمارستان، بیشتر از آن دسته داروها برای درمان بیماران استفاده می کنند.

McFarland Standards


OP-PE






mm
cm 1 2 3 4 6 7 8
mm
SXT
CIPR5
CTX30

Drug Resistance

- **MDR (Multi drug Resistant)**
- **XDR (Extensively drug Resistant)**
- **PDR (Pandrug Resistant)**
- **MRSA (Methicillin Resistant Staph aureus)**

- **VRE (Vancomycin Resistant Enterococci)**
- **CRE (Carbapenem Resistant Enterobacterales**
- **KPC (Klebsiella Pneumoniae Carbapenemase**
- **ESBL (Extended-Spectrum ß-Lactamase)**

ESBL

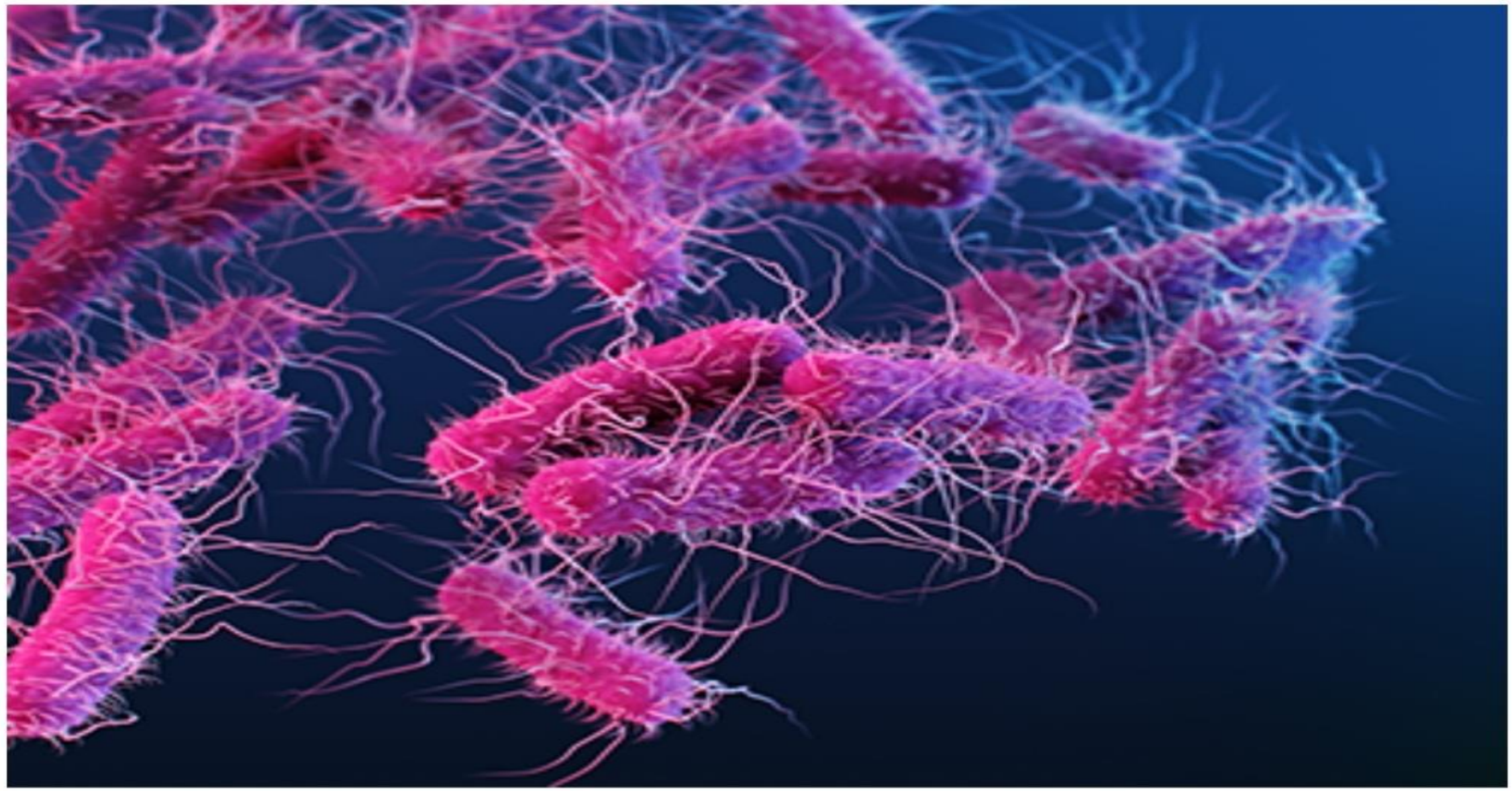
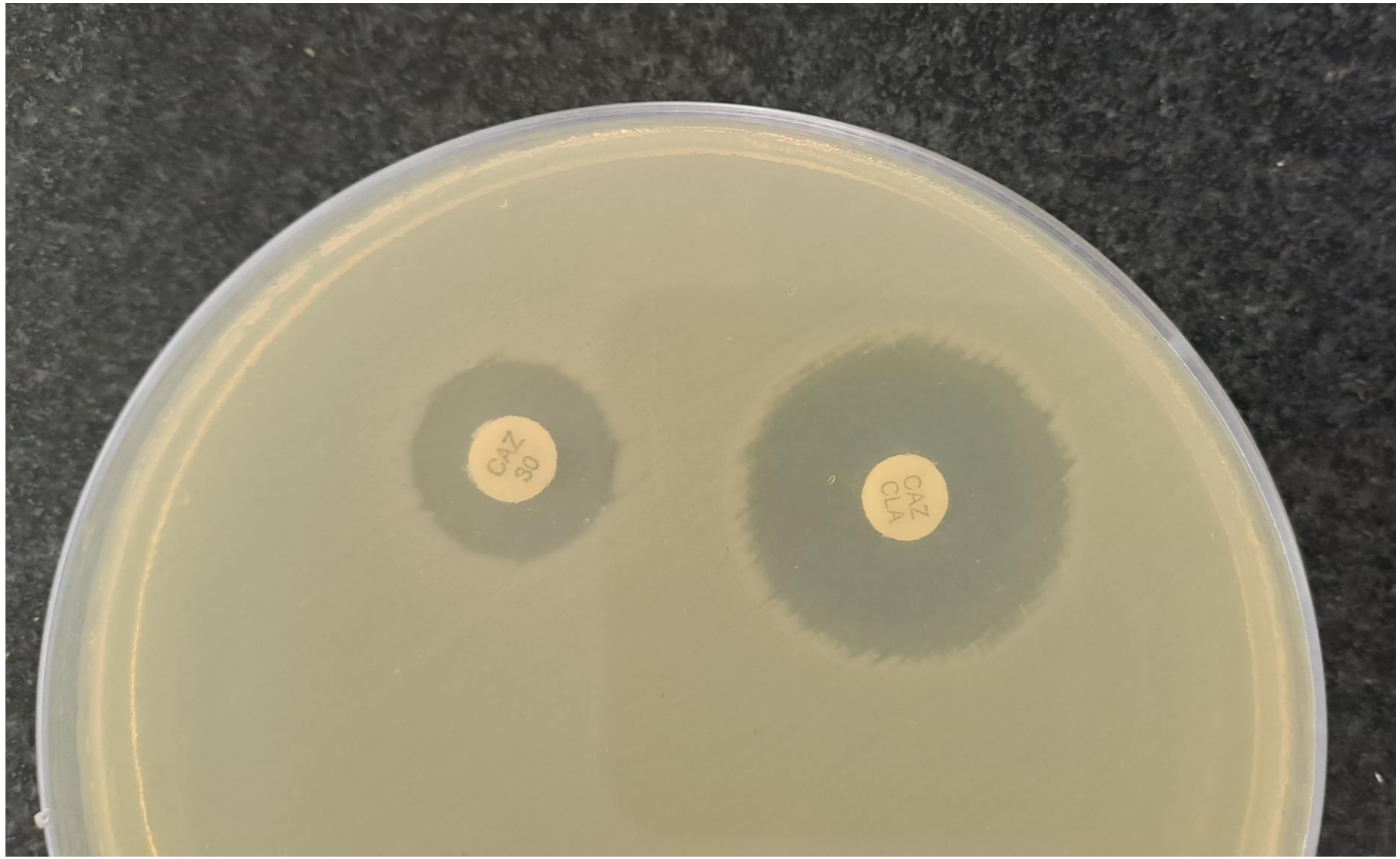


Table 3A. (Continued)

Test	Criteria for Performance of ESBL Test		ESBL Test	
Test method	Disk diffusion	Broth microdilution	Disk diffusion	Broth microdilution
Medium	MHA	CAMHB	MHA	CAMHB
Antimicrobial concentration	For *K. pneumoniae*, *K. oxytoca*, and *E. coli*: Cefpodoxime 10 µg or Ceftazidime 30 µg or Aztreonam 30 µg or Cefotaxime 30 µg or Ceftriaxone 30 µg For *P. mirabilis*: Cefpodoxime 10 µg or Ceftazidime 30 µg or Cefotaxime 30 µg (Testing more than one antimicrobial agent improves the sensitivity of ESBL detection.)	For *K. pneumoniae*, *K. oxytoca*, and *E. coli*: Cefpodoxime 4 µg/mL or Ceftazidime 1 µg/mL or Aztreonam 1 µg/mL or Cefotaxime 1 µg/mL or Ceftriaxone 1 µg/mL For *P. mirabilis*: Cefpodoxime 1 µg/mL or Ceftazidime 1 µg/mL or Cefotaxime 1 µg/mL (Testing more than one antimicrobial agent improves the sensitivity of ESBL detection.)	Ceftazidime 30 µg Ceftazidime-clavulanate[a] 30/10 µg and Cefotaxime 30 µg Cefotaxime-clavulanate 30/10 µg (Testing necessitates using both cefotaxime and ceftazidime, alone and in combination with clavulanate.)	Ceftazidime 0.25-128 µg/mL Ceftazidime-clavulanate 0.25/4-128/4 µg/mL and Cefotaxime 0.25-64 µg/mL Cefotaxime-clavulanate 0.25/4-64/4 µg/mL (Testing necessitates using both cefotaxime and ceftazidime, alone and in combination with clavulanate.)
Inoculum	Standard disk diffusion procedure	Standard broth dilution procedure	Standard disk diffusion procedure	Standard broth dilution procedure
Incubation conditions	35°C±2°C; ambient air	35°C±2°C; ambient air	35°C±2°C; ambient air	35°C±2°C; ambient air
Incubation length	16-18 hours	16-20 hours	16-18 hours	16-20 hours

Table 3A. (Continued)

Test	Criteria for Performance of ESBL Test		ESBL Test	
Test method	Disk diffusion	Broth microdilution	Disk diffusion	Broth microdilution
Results	For *K. pneumoniae*, *K. oxytoca*, and *E. coli*:	Growth at or above the concentrations listed may indicate ESBL production (ie, for *E. coli*, *K. pneumoniae*, and *K. oxytoca*, MIC ≥8 µg/mL for cefpodoxime or MIC ≥2 µg/mL for ceftazidime, aztreonam, cefotaxime, or ceftriaxone; and for *P. mirabilis*, MIC ≥2 µg/mL for cefpodoxime, ceftazidime, or cefotaxime).	A ≥5-mm increase in a zone diameter for either antimicrobial agent tested in combination with clavulanate vs the zone diameter of the agent when tested alone = ESBL (eg, ceftazidime zone = 16; ceftazidime-clavulanate zone = 21).	A ≥3 2-fold concentration decrease in an MIC for either antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone = ESBL (eg, ceftazidime MIC = 8 µg/mL; ceftazidime-clavulanate MIC = 1 µg/mL).
	Cefpodoxime zone ≤17 mm Ceftazidime zone ≤22 mm Aztreonam zone ≤27 mm Cefotaxime zone ≤27 mm Ceftriaxone zone ≤25 mm			
	For *P. mirabilis*:			
	Cefpodoxime zone ≤22 mm Ceftazidime zone ≤22 mm Cefotaxime zone ≤27 mm			
	Zones above may indicate ESBL production.			
Reporting			For all confirmed ESBL-producing strains: If laboratories use current cephalosporin and aztreonam breakpoints, test interpretations for these agents do not need to be changed from susceptible to resistant.	


CAZ
30
CAZ
CLA


با آرزوی موفقیت...