In the name of GOD

Standard Methods for AST
(Identification & Reporting of Resistant Strains)

Dr. Hadi Rezaei, PhD.

Clinical & Laboratory Bacteriologist

Founder & Director at Medical Lab

CLINICAL AND LABORATORY STANDARDS INSTITUTE

33rd Edition

M100

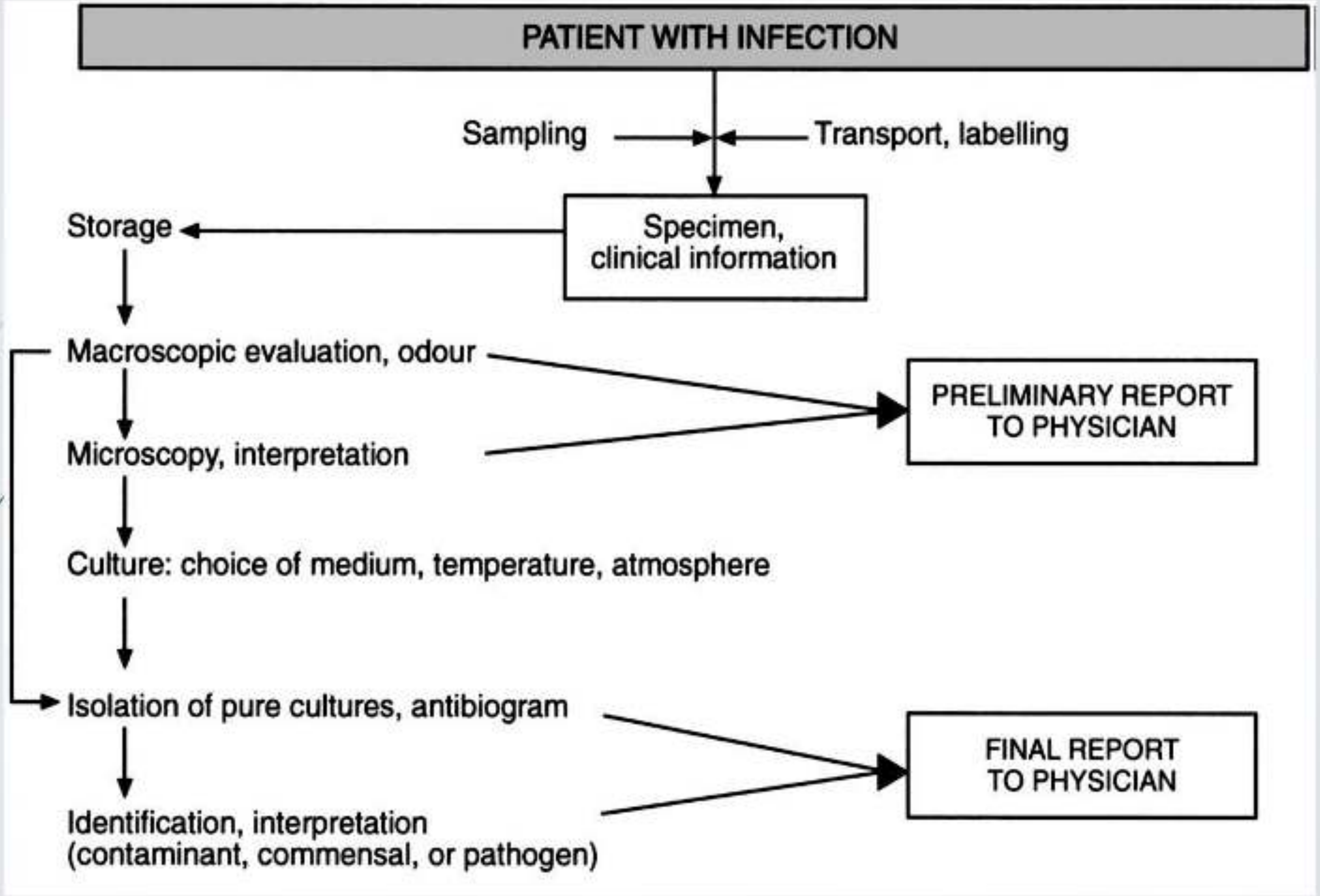
Performance Standards for Antimicrobial Susceptibility Testing

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

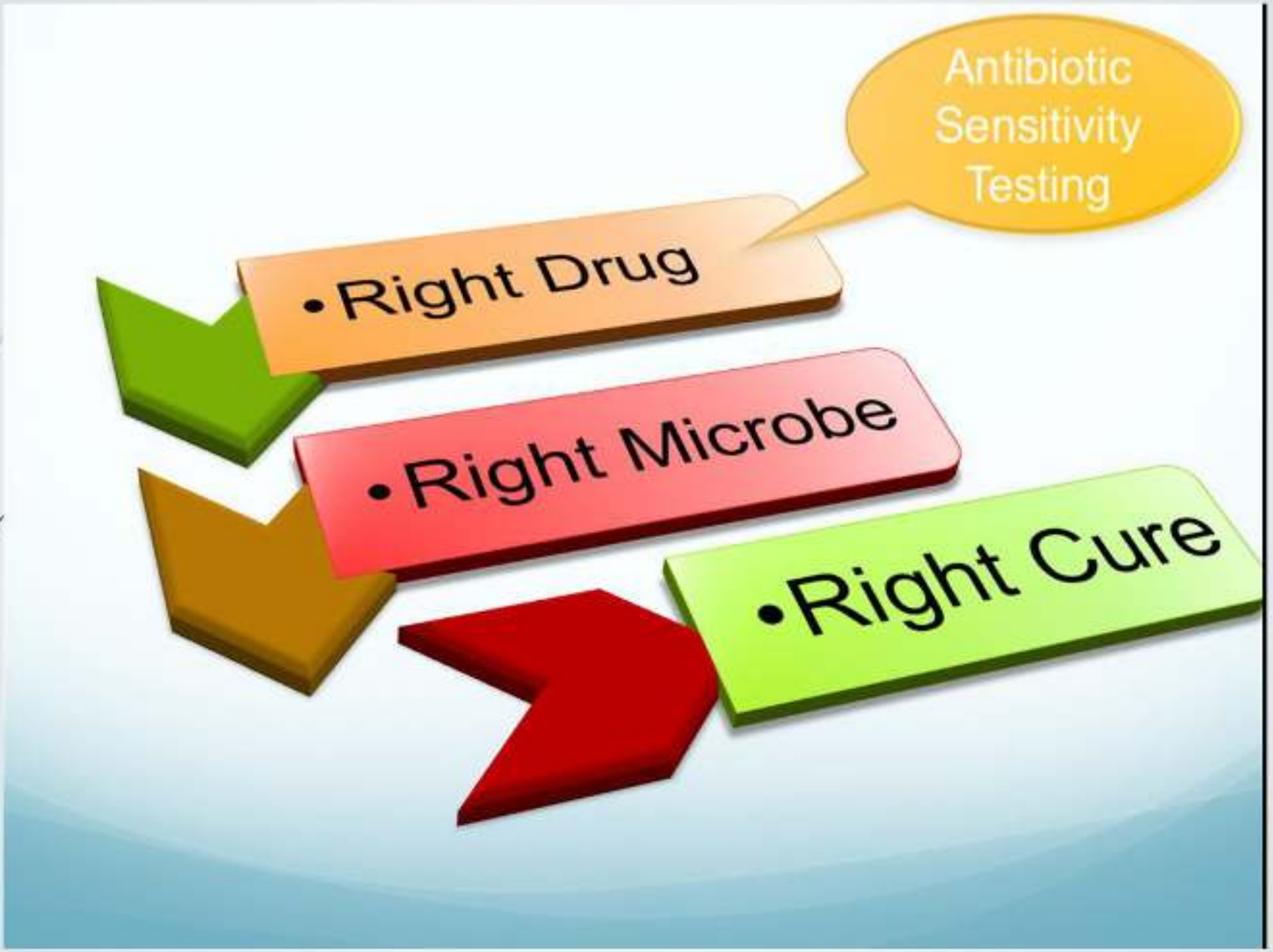
A CLSI supplement for global application.

Outline:

- ✓ Introduction
- ✓ Methods of Antimicrobial Susceptibility Testing (AST)
- ✓ Classification of Antibiotics
- ✓ CLSI and Important Definitions & Determinants (33rd Edition-2023)
- ✓ Criteria for Selective & Cascade Reporting
- ✓ Analysis and Interpretation of AST results
- ✓ Identification and Report of Resistant Strains
- ✓ Quality Assurance & Quality Control (QA&QC) in AST
- ✓ WHONET 2022 for Correct and Reliable Analysis of AST Results


PATIENT WITH INFECTION
Sampling
Transport, labelling
Specimen, clinical information
Storage
Macroscopic evaluation, odour
Microscopy, interpretation
PRELIMINARY REPORT TO PHYSICIAN
Culture: choice of medium, temperature, atmosphere
Isolation of pure cultures, antibiogram
Identification, interpretation (contaminant, commensal, or pathogen)
FINAL REPORT TO PHYSICIAN

AST is essential for the selection of the appropriate antibiotic


Antibiotic
Sensitivity
Testing
•Right Drug
•Right Microbe
•Right Cure

Purposes

- To guide the clinician in selecting the **best antibiotic** agent for an individual patient.
- To control the use of **inappropriate antibiotics** in clinical practice.
- To accumulate epidemiological information on the resistance of microorganisms of public health importance within the **community**.
- To reveal the **changing trends** in the local isolates.

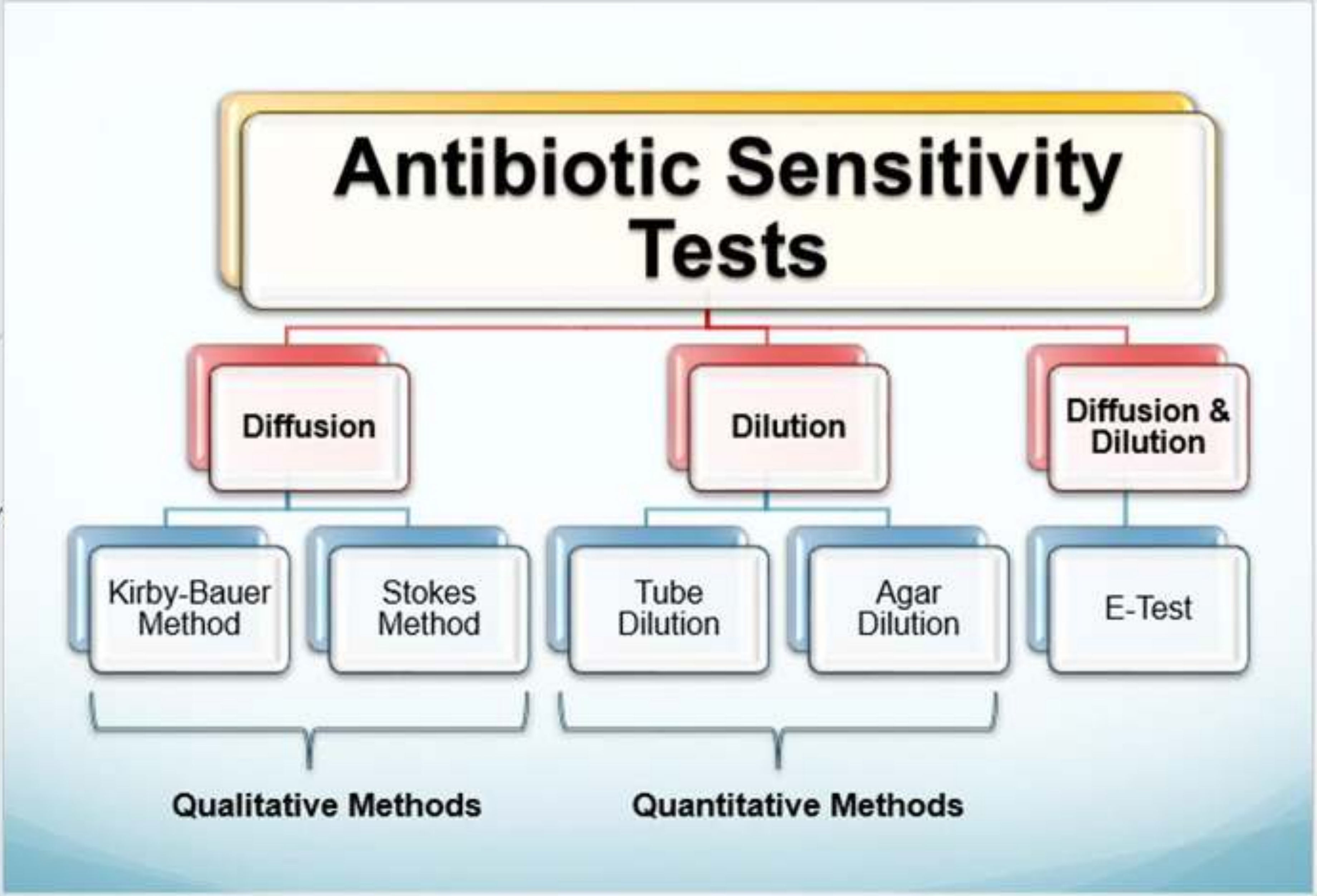
Types

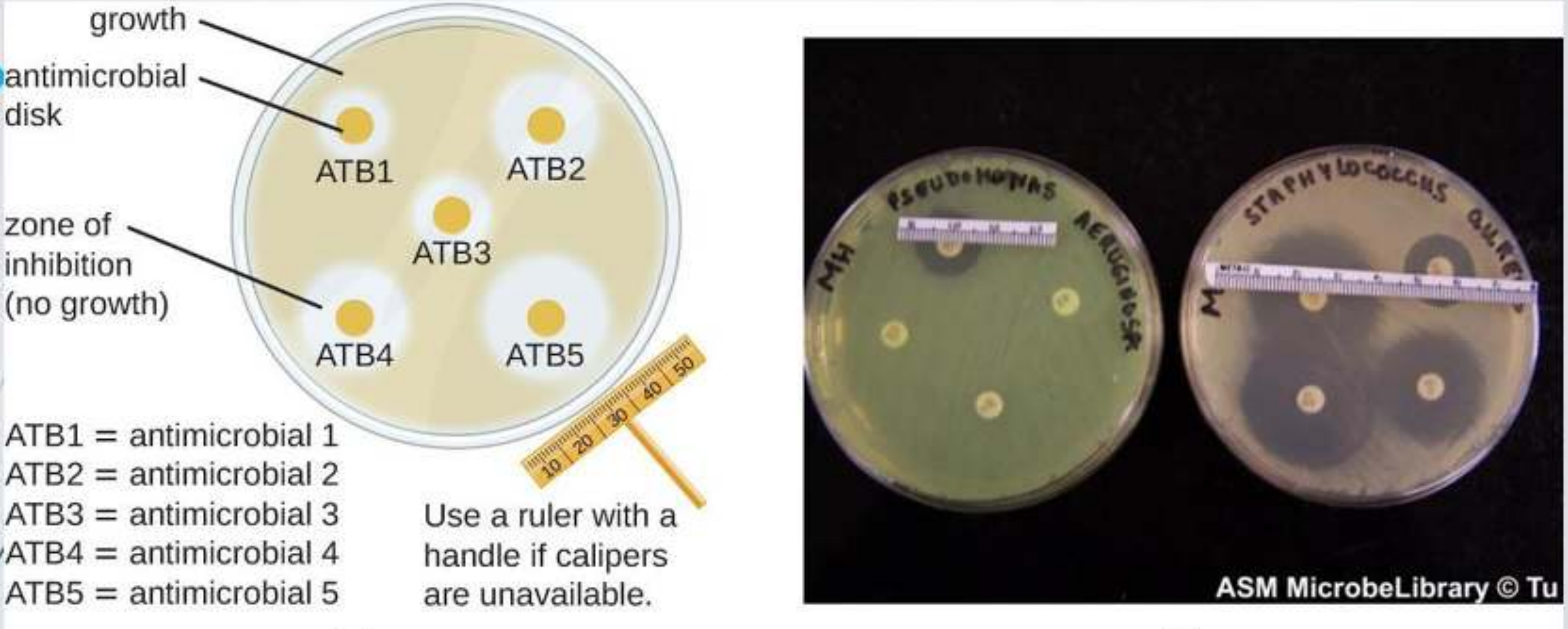
Qualitative

- For the testing of isolates from “healthy” patients with intact immune defenses.
- For **less serious infections** such as uncomplicated urinary tract infections.

Quantitative

- In the treatment of **serious infections** such as endocarditis or osteomyelitis.
- For infections in high-risk patient groups such as **immunocompromised** patients (*e.g.*. transplant patients).
- Those who are **critically ill**.


Antibiotic Sensitivity Tests
Diffusion
Dilution
Diffusion & Dilution
Kirby-Bauer Method
Stokes Method
Tube Dilution
Agar Dilution
E-Test
Qualitative Methods
Quantitative Methods

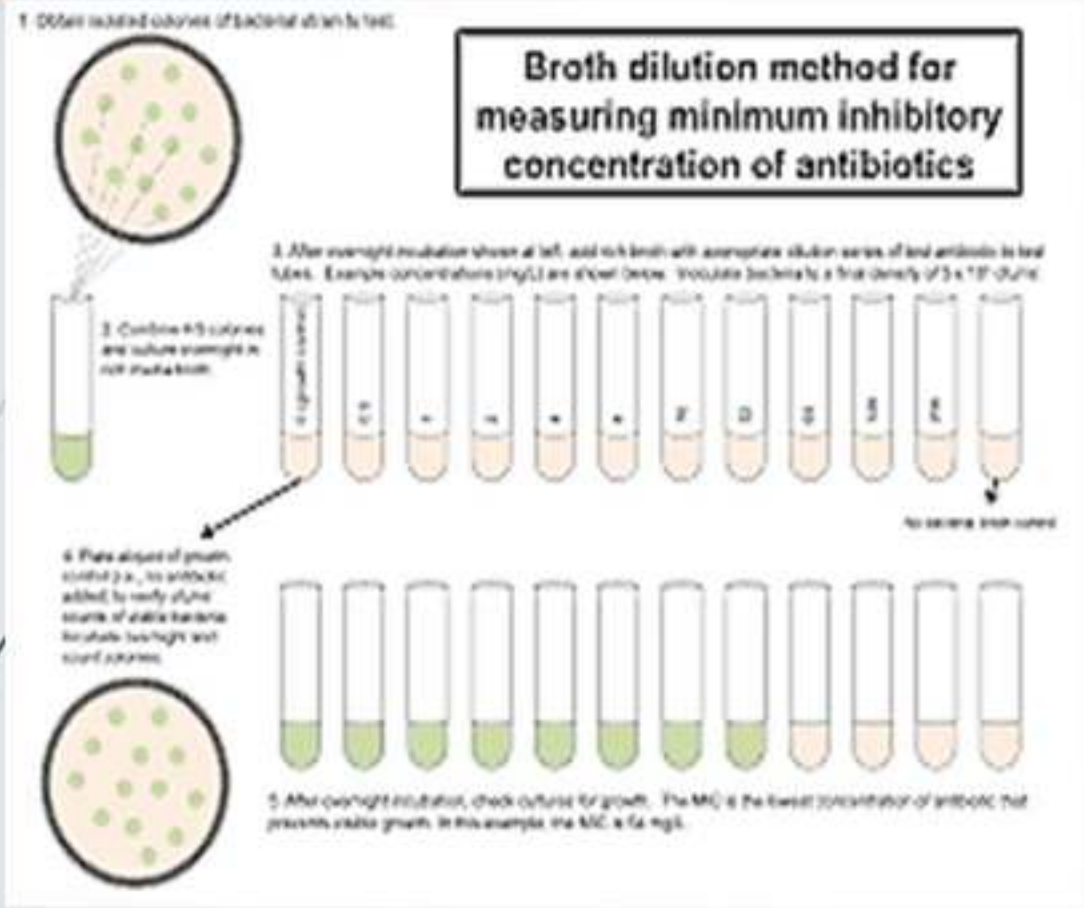

growth
antimicrobial disk
zone of inhibition (no growth)
ATB1
ATB2
ATB3
ATB4
ATB5
ATB1 = antimicrobial 1
ATB2 = antimicrobial 2
ATB3 = antimicrobial 3
ATB4 = antimicrobial 4
ATB5 = antimicrobial 5
10 20 30 40 50
Use a ruler with a handle if calipers are unavailable.
ASM MicrobeLibrary © Tu

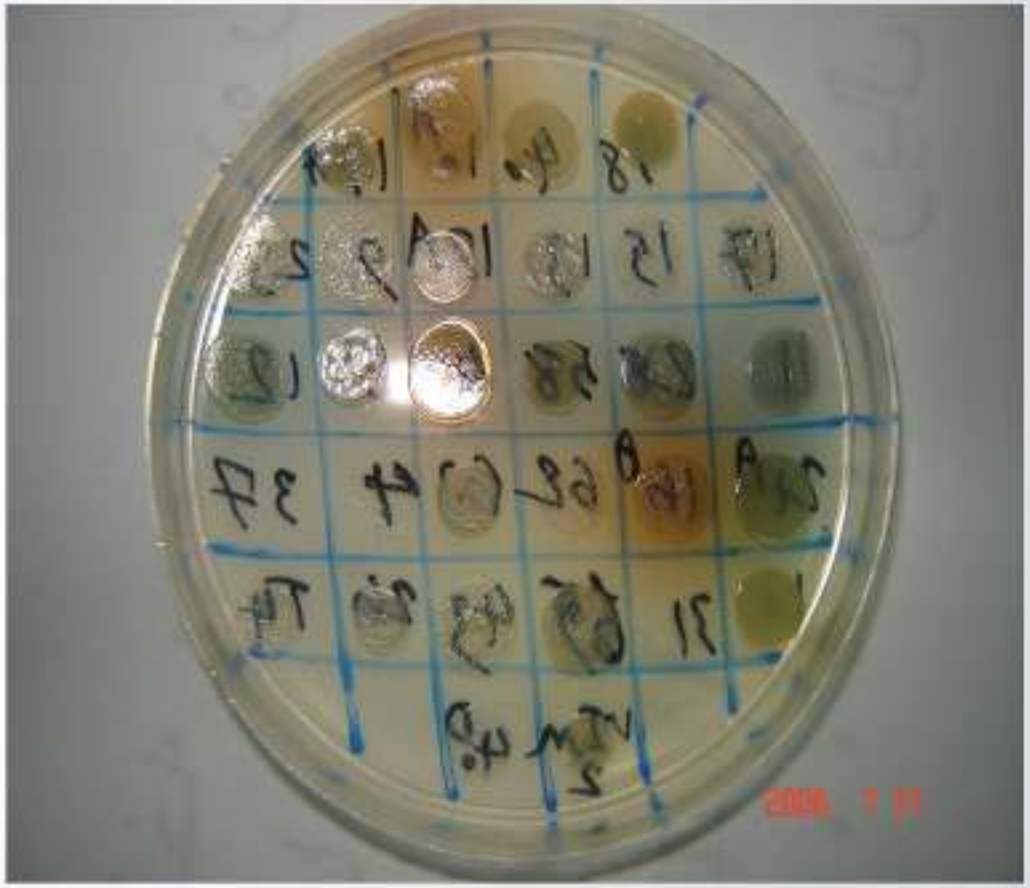
(a) (b)

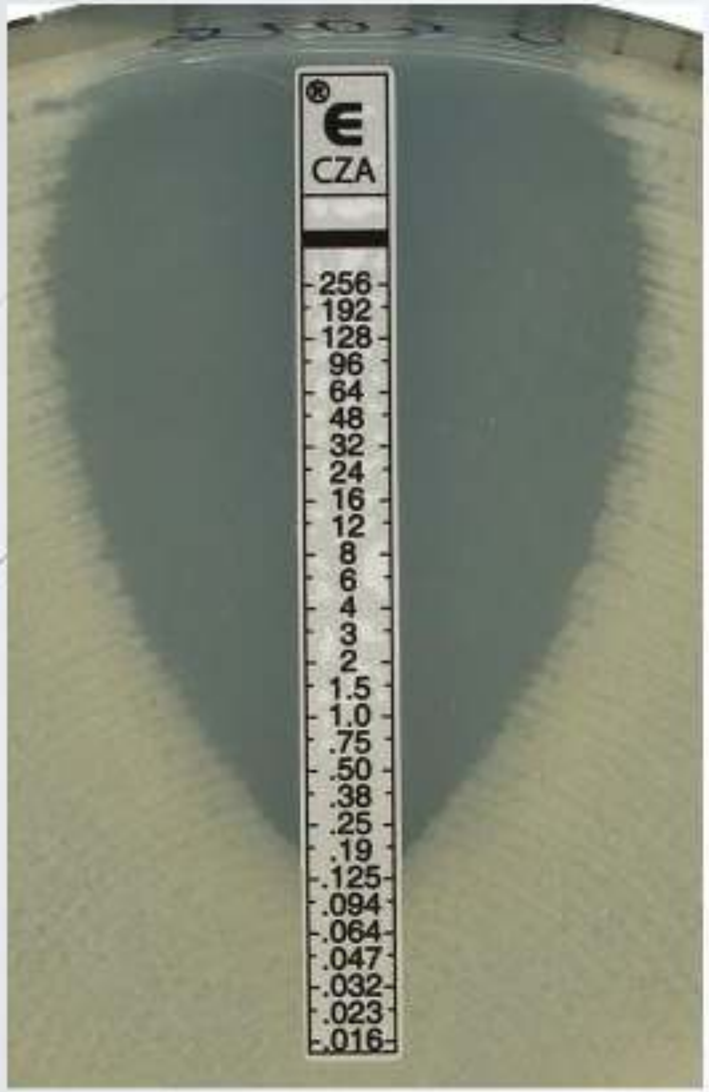
$$(1)\ \text{Weight (mg)} = \frac{\text{Volume (mL)} \cdot \text{Concentration (µg/mL)}}{\text{Potency (µg/mg)}}$$

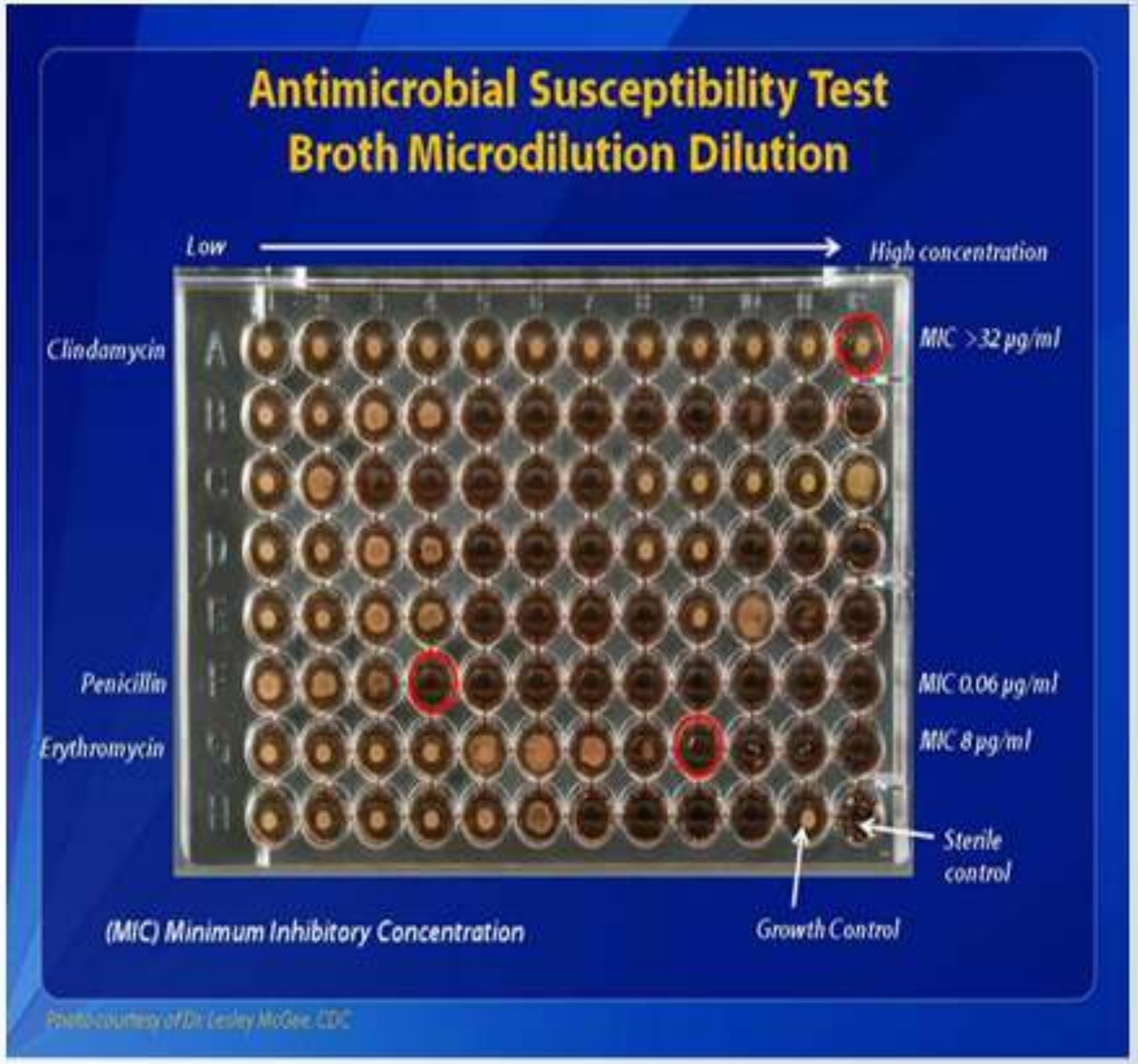
or

$$(2)\ \text{Volume (mL)} = \frac{\text{Weight (mg)} \cdot \text{Potency (µg/mg)}}{\text{Concentration (µg/mL)}}$$


Broth dilution method for measuring minimum inhibitory concentration of antibiotics




E
CZA
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


Antimicrobial Susceptibility Test
Broth Microdilution Dilution
Low
High concentration
Clindamycin
MIC >32 µg/ml
Penicillin
MIC 0.06 µg/ml
Erythromycin
MIC 8 µg/ml
Sterile control
Growth Control
(MIC) Minimum Inhibitory Concentration

Characteristics of the Ideal Antimicrobial Drugs

- Selectively toxic to the microbe but nontoxic to host cells
- Microbicidal rather than microbistatic
- Relatively soluble; functions even when highly diluted in body fluids
- Remains potent long enough to act and is not broken down or excreted prematurely
- Doesn't lead to the development of antimicrobial resistance
- Complements or assists the activities of the host's defenses
- Remains active in tissues and body fluids
- Readily delivered to the site of infection
- Reasonably priced
- Does not disrupt the host's health by causing allergies or predisposing the host to other infections

Classification of Antibiotics

- **Classification on Mechanisms of Action:**

1. Interference with cell membrane structure or function
2. Inhibition of cell wall synthesis
3. Inhibition of protein synthesis
4. Inhibition of Nucleic Acid Synthesis (DNA & RNA)
5. Antimetabolite Antibiotics

Targets of Antimicrobials

Cell wall inhibitors

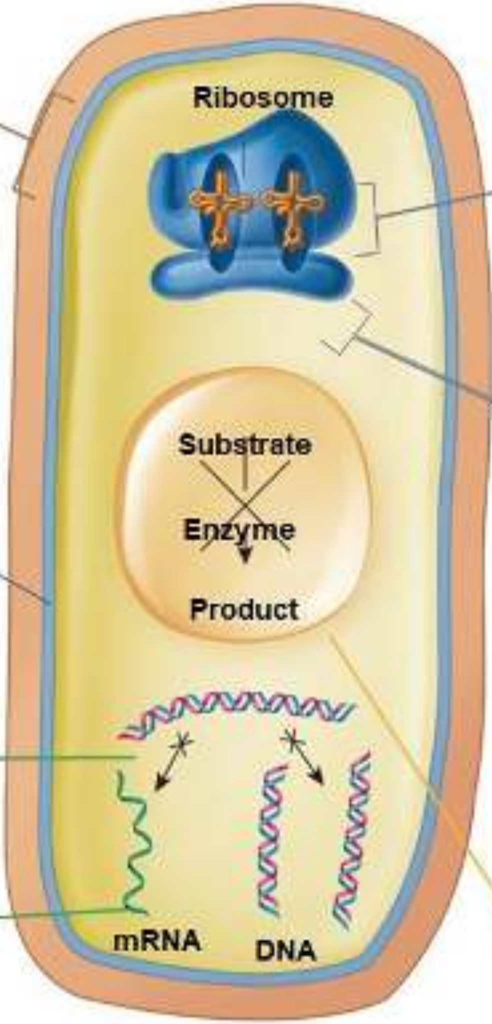
Block synthesis and repair
1. β-Lactams
2. Glycopeptids
3. Bacitracin
4. Fosfomycin
5. Isoniazid
6. Ethambutol
7. Cycloserine
8. Moenomycin

Cell membrane

Polymyxins
Daptomycin
Nystatin

DNA/RNA

Quinolones
Rifamycins
Metronidazole
Clofazimine
Novobiocin



Protein synthesis inhibitors acting on ribosomes

Site of action 50S subunit

Macrolides
chloramphenicol

Site of action 30S subunit

Aminoglycosides
Tetracyclines
Glycylcyclines

Both 30S and 50S

Blocks initiation of protein synthesis
Linezolid

Antimetabolite (Folic acid synthesis)

Block pathways and inhibit metabolism
Sulfonamides (sulfa drugs)
Trimethoprim
Dapson

Antimicrobial Class	Antimicrobial Subclass(es)		Agent(s) Included; Generic Name(s)
Penicillins	Penicillinase-labile penicillins[a]	Penicillin	Penicillin
		Aminopenicillins	Amoxicillin Ampicillin
		Carboxypenicillins	Carbenicillin Ticarcillin
		Ureidopenicillins	Azlocillin Mezlocillin Piperacillin
	Penicillinase-stable penicillins[b]		Cloxacillin Dicloxacillin Methicillin Nafcillin Oxacillin
	Aminopenicillin		Mecillinam
β-lactam combination agents			Amoxicillin-clavulanate Ampicillin-sulbactam Aztreonam-avibactam Cefepime-tazobactam **(1:1)** **Cefepime-zidebactam** Ceftaroline-avibactam Ceftazidime-avibactam Ceftolozane-tazobactam Imipenem-relebactam Meropenem-vaborbactam Piperacillin-tazobactam Ticarcillin-clavulanate
Cephems (parenteral)	Cephalosporins I[c]		Cefazolin Cephalothin Cephapirin Cephradine
	Cephalosporins II[c]		Cefamandole Cefonicid Cefuroxime (parenteral)
	Cephalosporins III[c]		Cefoperazone Cefotaxime Ceftazidime Ceftizoxime Ceftriaxone
	Cephalosporins IV[c]		Cefepime Cefpirome

Antimicrobial Class	Antimicrobial Subclass(es)	Agent(s) Included; Generic Name(s)
Cephems (parenteral (Continued)	Cephalosporins with anti-MRSA activity	Ceftaroline Ceftobiprole
	Cephamycins	Cefmetazole Cefotetan Cefoxitin
	Oxacephem	Moxalactam
	Siderophore cephalosporin	**Cefiderocol**
Cephems (oral)	Cephalosporins	Cefaclor Cefadroxil Cefdinir Cefditoren Cefetamet Cefixime Cefpodoxime Cefprozil Ceftibuten Cefuroxime (oral) Cephalexin Cephradine
	Carbacephem	Loracarbef
Monobactams		Aztreonam
Penems	Carbapenems	Biapenem Doripenem Ertapenem Imipenem Meropenem Razupenem
	Penems	Faropenem Sulopenem

Antimicrobial Class	Antimicrobial Subclass(es)	Agent(s) Included; Generic Name(s)
Aminocyclitols		Spectinomycin
Aminoglycosides		Amikacin Gentamicin Kanamycin Netilmicin Plazomicin Streptomycin Tobramycin
Aminoglycoside-fosfomycin		Amikacin-fosfomycin
Ansamycins	**Rifamycins**	**Rifabutin** **Rifapentine** Rifampin Rifaximin
Folate pathway antagonists	**Dihydrofolate reductase inhibitors**	Iclaprim Sulfonamides Trimethoprim Trimethoprim-sulfamethoxazole
	Sulfonamides	Sulfamethoxazole Sulfisoxazole
	Combination	Trimethoprim-sulfamethoxazole
Fosfomycins		Fosfomycin
Glycopeptides	Glycopeptide	Vancomycin
	Lipoglycopeptides	Dalbavancin Oritavancin Teicoplanin Telavancin Ramoplanin
Lincosamides		Clindamycin Lincomycin
Lipopeptides		Daptomycin Surotomycin
	Polymyxins	Colistin Polymyxin B
Macrocyclic lactone		Fidaxomicin

Antimicrobial Class	Antimicrobial Subclass(es)	Agent(s) Included; Generic Name(s)
Macrolides		Azithromycin Clarithromycin Dirithromycin Erythromycin
	Fluoroketolide	Solithromycin
	Ketolides	Nafithromycin Telithromycin
Nitroheterocyclics	**Nitrofuran**	Nitrofurantoin
	Nitroimidazoles	Metronidazole Secnidazole Tinidazole
	Thiazolides	**Nitazoxanide** **Tizoxanide**
Oxazolidinones		Linezolid Tedizolid
Peptide	Magainin	Pexiganan
Phenicols		Chloramphenicol **Thiamphenicol**
Pleuromutilins		Lefamulin **Retapamulin**
Pseudomonic acid		Mupirocin
Quinolones		Cinoxacin Garenoxacin Nalidixic acid
	Benzoquinolizine	Levonadifloxacin
	Fluoroquinolones	Besifloxacin Ciprofloxacin Clinafloxacin Delafloxacin Enoxacin Finafloxacin Fleroxacin Gatifloxacin Gemifloxacin Grepafloxacin Levofloxacin Lomefloxacin Moxifloxacin Norfloxacin Ofloxacin Pefloxacin Sparfloxacin Trovafloxacin Ulifloxacin (prulifloxacin)

Antimicrobial Class	Antimicrobial Subclass(es)	Agent(s) Included; Generic Name(s)
Quinolonyl oxazolidinone		Cadazolid
Steroid	Fusidane	Fusidic acid
Streptogramins		Quinupristin-dalfopristin
Tetracyclines		Doxycycline Minocycline Tetracycline
	Fluorocycline	Eravacycline
	Glycylcycline	Tigecycline
	Aminomethylcycline	Omadacycline
Triazaacenaphthylene		Gepotidacin

What are factors promote antimicrobial resistance?

- ✓ Exposure to sub-optimal levels of antimicrobial
- ✓ Inappropriate use
- ✓ Exposure to microbes carrying resistance genes

Inappropriate Antimicrobial Use

- Prescription not taken correctly
- Antibiotics for viral infections
- Antibiotics sold without medical supervision
- Spread of resistant microbes in hospitals due to lack of hygiene


CAUSES OF
ANTIBIOTIC RESISTANCE
HANDLE ANTIBIOTICS WITH CARE
Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.
Over-prescribing of antibiotics
Patients not finishing their treatment
Over-use of antibiotics in livestock and fish farming
Poor infection control in hospitals and clinics
Lack of hygiene and poor sanitation
Lack of new antibiotics being developed
www.who.int/drugresistance
#AntibioticResistance
World Health Organization

ANTIBIOTIC RESISTANCE WHAT YOU CAN DO

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

1. Only use antibiotics when **prescribed** by a certified health professional
2. Always take the **full prescription**, even if you feel better
3. **Never use left over** antibiotics
4. **Never share** antibiotics with others
5. **Prevent infections** by regularly washing your hands, avoiding contact with sick people and keeping your vaccinations up to date

www.who.int/drugresistance

#AntibioticResistance

World Health Organization

ANTIBIOTIC RESISTANCE WHAT POLICY MAKERS CAN DO

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

1. Ensure you have a robust **national action plan** to tackle antibiotic resistance
2. Improve **surveillance** of antibiotic-resistant infections
3. Strengthen **infection prevention** and control measures
4. **Regulate and promote** the appropriate use of quality medicines
5. Make information on the **impact** of antibiotic resistance available

www.who.int/drugresistance

#AntibioticResistance

World Health Organization

ANTIBIOTIC RESISTANCE WHAT HEALTH WORKERS CAN DO

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

1. **Prevent infections** by ensuring your hands, instruments and environment are clean
2. Keep your patients' **vaccinations** up to date
3. If you think a patient might need antibiotics, where possible, **test to confirm** and find out which one
4. Only prescribe and dispense antibiotics when they are **truly needed**
5. Prescribe and dispense **the right antibiotic at the right dose for the right duration**

www.who.int/drugresistance

#AntibioticResistance

World Health Organization

ANTIBIOTIC RESISTANCE
WHAT THE AGRICULTURE SECTOR CAN DO

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

1. Ensure that antibiotics given to animals—including food-producing and companion animals—are **only used to control or treat** infectious diseases and under veterinary supervision
2. **Vaccinate** animals to reduce the need for antibiotics and **develop alternatives** to the use of antibiotics in plants
3. Promote and apply **good practices** at all steps of production and processing of foods from animal and plant sources
4. Adopt **sustainable systems** with improved hygiene, biosecurity and stress-free handling of animals
5. Implement **international standards** for the responsible use of antibiotics and guidelines, set out by OIE, FAO and WHO

www.who.int/drugresistance
www.oie.int/antimicrobial-resistance
www.fao.org/antimicrobial-resistance

#AntibioticResistance

Food and Agriculture Organization of the United Nations

OIE WORLD ORGANISATION FOR ANIMAL HEALTH

World Health Organization

Clinical & Diagnostic Microbiology Lab

- ✓ Isolation, purification and identification of microbes from clinical specimens
- ✓ AST on standard protocols with QA & QC
- ✓ Selection of type of AST (qualitative or quantitative or both)
- ✓ Selection of best and suitable antibiotics
- ✓ Accurate analysis and interpretation of AST results
- ✓ Identification and detection of important resistant strains:
  - ➢ MRSA,MR-CoNS, VISA, VRSA, VRE, ESBL, MDR, XDR, PDR , etc.
- ✓ Rapid and timely reporting of AST results (Critical results)

Test/Report Tiers and Additional Designations (CLSI; 2023)

Antimicrobial Agent Test and Report Tiers and Additional Considerations for Agents Listed in Tables 1

Tier	Definition	Test	Report[a]	Additional Testing and Reporting Considerations
1	Antimicrobial agents that are appropriate for routine, primary testing and reporting	Routine	Routine	
2	Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Routine	Cascade[b]	• Report following cascade reporting rules due to resistance to agent(s) in Tier 1. • May be reported routinely based on institution-specific guidelines.
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[c]	Routine or by request	Cascade[b]	Test routinely based on institution-specific guidelines or by clinician request and report following cascade reporting rules due to resistance to agent(s) in Tiers 1 and 2.

Antimicrobial Agent Test and Report Tiers and Additional Considerations for Agents Listed in Tables 1 (Continued)

Tier	Definition	Test	Report[a]	Additional Testing and Reporting Considerations
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	By request	By request	• Test and report by clinician request due to: – Unavailability of preferred drug for clinical use – Patient underlying condition, including allergies – Unusual susceptibility profile of the organism, including resistance to agents in Tiers 1, 2, and 3 – Polymicrobial infection • May also warrant testing as an epidemiological aid (eg, testing ceftazidime for Enterobacterales to indicate potential extended-spectrum ß-lactamase production; see Table 3A).
Urine only	Antimicrobial agents designated by a "(U)" in Tables 2 should be reported only on organisms isolated from the urinary tract.	Routine	Report as appropriate	Agents in Tiers 1, 2, and 3 may also be reported on urine isolates, as appropriate, following the testing and reporting guidance for the respective tiers.

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

Antimicrobial Agent Test and Report Designations and Additional Considerations for Agents Not Listed in Tables 1

Designation	Definition	Test	Report[a]	Additional Testing and Reporting Considerations
Other	Antimicrobial agents with established clinical breakpoints designated by an * in Tables 2 that are generally not candidates for testing and reporting in the United States	By request	By request	Test and report only by clinician request and only following consultation with the antimicrobial stewardship team and other relevant institutional stakeholders to ensure appropriateness of the request. Agents with an "Other" designation may not reflect current consensus recommendations for first-choice and alternative drugs for the specific organism or organism group.
Inv.	Antimicrobial agents that are investigational for the organism group designated by "Inv." in Tables 2 have not yet been approved by the FDA for use in the United States.	By request	By request	Test and report only by clinician request and only following consultation with the antimicrobial stewardship team and other relevant institutional stakeholders to ensure appropriateness of the request. These agents would likely be clinically available for compassionate use only.

Abbreviations: FDA, US Food and Drug Administration; UTI, urinary tract infection.

Tiers 1,2,3,4 /<u>U</u>rine /Other<u>*</u>/<u>Inv</u>

Tables 1A–1P: For Testing and Reporting by Microbiology Laboratories:

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	Cefiderocol	
	Imipenem	Ceftazidime-avibactam	
	Meropenem	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 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 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.

Example: Enterobacterales; Tables 1A & 2A

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	Cefiderocol	
	Imipenem	Ceftazidime-avibactam	
	Meropenem	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 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 ß-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.

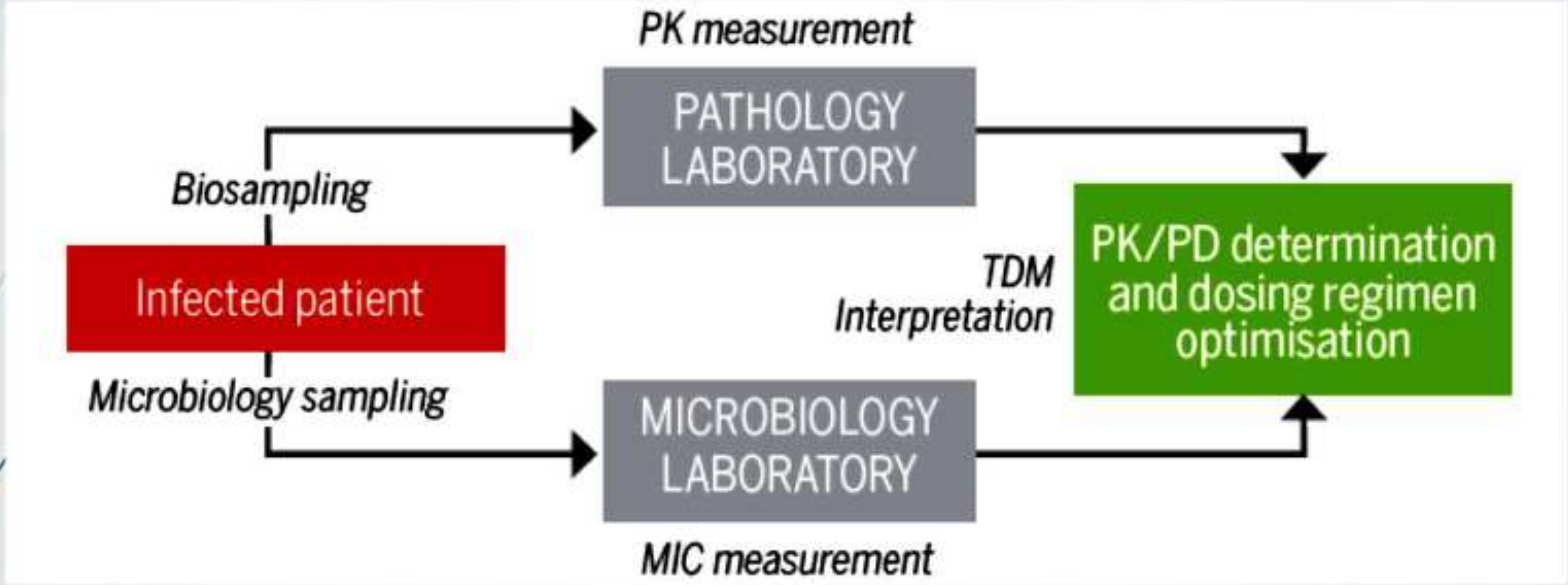
Symbols: ^, designation for agents that have the potential to concentrate in the urine; ***, designation for "Other" agents that are not included in Tables 1 but have established clinical breakpoints.**

<u>Footnotes</u>

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

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

Breakpoint and Interpretive Category Definitions



Breakpoint and Interpretive Category Definitions

- ✓ Susceptible(S)
- ✓ Susceptible-dose dependent (SDD)
- ✓ Intermediate(I)
- ✓ Resistant(R)
- ✓ Nonsusceptible(NS)

Susceptible-dose dependent (SDD)

- A category defined by a breakpoint that implies that susceptibility of an isolate depends on the dosage regimen that is used in the patient.

- To achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either MICs or zone diameters) are in the SDD category, it is necessary to use a dosage regimen:
  - higher doses,
  - more frequent doses
  - extended infusion or both
- that results in higher drug exposure than that achieved with the dose that was used to establish the susceptible breakpoint..

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).

Appendix E. (Continued)

Antimicrobial Agent	Breakpoints and Interpretive Categories: Susceptible MIC	Susceptible Dose	SDD MIC	SDD Dose
Table 2A. Enterobacterales (Continued)				
Cefepime	≤ 2 µg/mL	1 g administered every 12 h	4 µg/mL	1 g administered every 8 h or 2 g administered every 12 h
			8 µg/mL or zone diameter: 19-24 mm	2 g administered every 8 h (Because it is not possible to correlate specific zone diameters with specific MICs, an isolate with a zone diameter in the SDD range should be treated as if it might be an MIC of 8 µg/mL.)
Cefiderocol	≤ 4 µg/mL	2 g every 8 h administered over 3 h	N/A	
Cefotaxime	≤ 1 µg/mL	1 g administered every 8 h	N/A	
Ceftriaxone	≤ 1 µg/mL	1 g administered every 24 h	N/A	
Cefoxitin	≤ 8 µg/mL	8 g per day (eg, 2 g administered every 6 h)	N/A	
Cefuroxime	≤ 8 µg/mL	1.5 g administered every 8 h	N/A	
[illegible]	[illegible]	[illegible]	[illegible]	

Nonsusceptible(NS)

- A category used for isolates for which only a susceptible breakpoint is designated because of the absence or rare occurrence of resistant strains.
- An isolate that is interpreted as nonsusceptible does not necessarily mean that the isolate has a resistance mechanism.
- It is possible that isolates lack resistance mechanisms may be encountered within the wild-type distribution after the time the susceptible-only breakpoint was set.
- The term "nonsusceptible" should not be used when the text is describing an organism/drug category with intermediate and resistant interpretive categories.
- Isolates that are in the categories of "intermediate" or "resistant" could be called "not susceptible" rather than "nonsusceptible."

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

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			
		S	I	R	S	I	R	
PENICILLINS								
(7) An organism that is susceptible to penicillin can be c[illegible]red susceptible to antimicrobial agents listed here when used for appr tested against those agents. For groups A, B, C, and G ß-he[illegible]ytic streptococci, penicillin is tested as a surrogate for ampicillin, amo sulbactam, cefazolin, cefepime, ceftaroline, cephradine, cephalothin, cefotaxime, ceftriaxone, ceftizoxime, imipenem, ertapenem, ß-hemolytic streptococci, penicillin is also a surrogate for cefaclor, cefdinir, cefprozil, ceftibuten, cefuroxime, and cefpodoxime.								
Penicillin or	10 units	≥24	-	-	≤0.12	-	-	See general co
ampicillin	10 µg	≥24	-	-	≤0.25	-	-	
CEPHEMS (PARENTERAL) (Including cephalosp[illegible] I, II, III, and IV. Please refer to Glossary I.)								
See comment (7).								
Cefepime or	30 µg	≥24	-	-	≤0.5	-	-	
cefotaxime or	30 µg	≥24	-	-	≤0.5	-	-	
ceftriaxone	30 µg	≥24	-	-	≤0.5	-	-	
Ceftaroline	30 µg	≥26	-	-	≤0.5	-	-	**(8)** Breakpoints administered e
CARBAPENEMS								
See comment (7).								
Doripenem*	-	-	-	-	≤0.12	-	-	
Ertapenem*	-	-	-	-	≤1	-	-	
Meropenem*	-	-	-	-	≤0.5	-	-	
GLYCOPEPTIDES								
Vancomycin	30 µg	≥17	-	-	≤1	-	-	
LIPOGLYCOPEPTIDES								
Dalbavancin	-	-	-	-	≤0.25	-	-	**(9) Report onl** *S. dysgalactiae*

Agents without Zone diameter breakpoints

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 ≤2	≥4 ≥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).

Not Applicable

Table 2C. *Staphylococcus* spp. (Continued)

Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm: S	SDD	I	R	Interpretive Categories and MIC Breakpoints, µg/mL: S	SDD	I	R	Comments
GLYCOPEPTIDES											
(22) MIC tests should be performed to determine the susceptibility of all isolates of staphylococci to vancomycin. The disk test does not differentiate vancomycin-susceptible isolates of *S. aureus* from vancomycin-intermediate isolates, nor does the test differentiate among vancomycin-susceptible, -intermediate, and -resistant isolates of *Staphylococcus* spp. other than *S. aureus*, all of which give similar size zones of inhibition.											
Vancomycin	*S. aureus*, including MRSA	-	-	-	-	-	≤2	-	4-8	≥16	**(23)** For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy. **(24)** Send any *S. aureus* for which the vancomycin is ≥8 µg/mL to a referral laboratory. See Appendix A. Also refer to Table 3G-1 for *S. aureus*, Subchapter 3.12 in M07,[4] and Subchapter 3.9 in M02.[1]
	Staphylococcus spp. other than *S. aureus*	-	-	-	-	-	≤4	-	8-16	≥32	**(25)** Send any *Staphylococcus* spp. other than *S. aureus* for which the vancomycin MIC is ≥32 µg/mL to a referral laboratory. See Appendix A. See also Subchapter 3.12 in M07[4] and Subchapter 3.9 in M02.[1]
LIPOGLYCOPEPTIDES											
Dalbavancin	*S. aureus*, including MRSA	-	-	-	-	-	≤0.25	-	-	-	**(26)** Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes.
Oritavancin		-	-	-	-	-	≤0.12	-	-	-	**(27)** Breakpoints are based on a dosage regimen of 1200 mg IV administered once.
Telavancin		-	-	-	-	-	≤0.12	-	-	-	**(28)** Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h.
Teicoplanin **(Inv.)**	All staphylococci	-	-	-	-	-	≤8	-	16	≥32	

Not Applicable

Selective and Cascade Reporting

- Each laboratory should consider developing selective and/or cascade reporting rules in consultation with the antimicrobial stewardship team and other relevant institutional stakeholders.

- Selective and cascade reporting is done to encourage appropriate antimicrobial agent use.

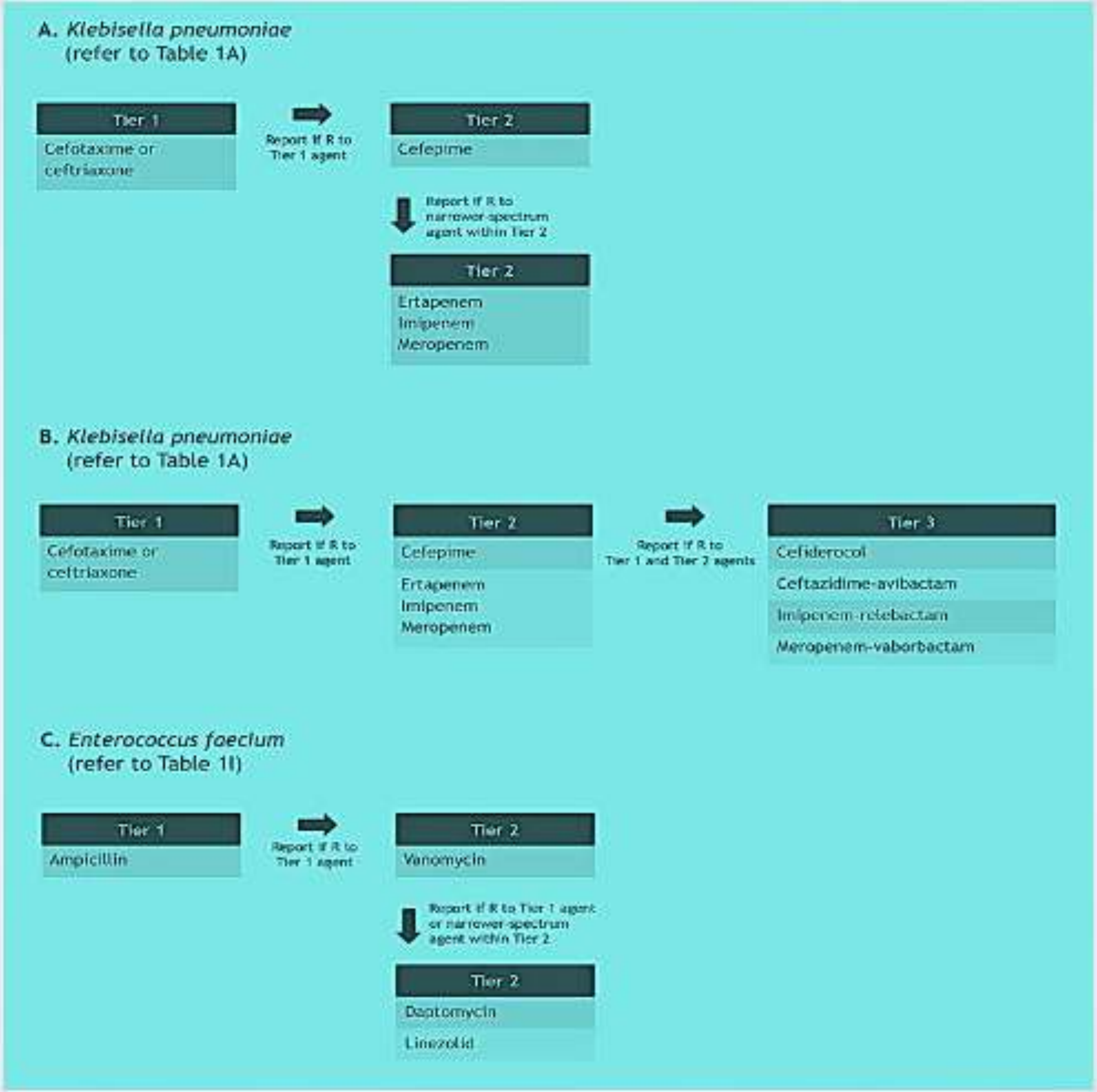
- **Selective reporting involves reporting results for specific antimicrobial agents based on defined criteria unrelated to results obtained from antimicrobial susceptibility testing (AST) :**

  - ✓ **organism identification**
  - ✓ **body site, (Type of specimen and infection site)**
  - ✓ **antibiotic therapy and types of antibiotics**
  - ✓ **patient demographics**
  - ✓ **patient information and history**
  - ✓ **hospitalized or community patients**
  - ✓ **nosocomial infections**

- For example:
  - Nitrofurantoin would be reported only on isolates from urine because it is effective in treating uncomplicated urinary tract infections (UTIs) only.
  - First- and second-generation cephalosporins are not reported on *Salmonella* spp. because of their ineffectiveness in treating patients with *Salmonella* infections.
- Results for secondary or broader-spectrum agents (eg, Tier 2 or 3) are reported only if the isolate is resistant to primary or narrower-spectrum agents (eg, Tier 1).
- For example:
  - If a *Klebsiella pneumoniae* isolate is resistant to ceftriaxone, cefepime might be reported.
  - ***A “resistant” result for a broader-spectrum agent (eg, Tier 2) should always be reported even if the organism tests “susceptible” to the narrower-spectrum agent (eg, Tier 1). Such unexpected resistant results should be confirmed.

- **Each laboratory should develop a protocol to test additional agents on isolates that are confirmed as resistant to all agents on their routine test panels.**

- **This protocol should include options for testing additional agents in-house or sending the isolate to a referral laboratory.**


A. Klebisella pneumoniae
(refer to Table 1A)
Tier 1
Cefotaxime or ceftriaxone
Report if R to Tier 1 agent
Tier 2
Cefepime
Report if R to narrower-spectrum agent within Tier 2
Tier 2
Ertapenem
Imipenem
Meropenem
B. Klebisella pneumoniae
(refer to Table 1A)
Tier 1
Cefotaxime or ceftriaxone
Report if R to Tier 1 agent
Tier 2
Cefepime
Ertapenem
Imipenem
Meropenem
Report if R to Tier 1 and Tier 2 agents
Tier 3
Cefiderocol
Ceftazidime-avibactam
Imipenem-relebactam
Meropenem-vaborbactam
C. Enterococcus faecium
(refer to Table 1I)
Tier 1
Ampicillin
Report if R to Tier 1 agent
Tier 2
Vanomycin
Report if R to Tier 1 agent or narrower-spectrum agent within Tier 2
Tier 2
Daptomycin
Linezolid

AST Results

(Analysis, Interpretation & Report)

General comments & Warning

Table 2B-1. Zone Diameter and MIC Breakpoints for *Pseudomonas aeruginosa*

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 [7]).

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)

Pseudomonas aeruginosa ATCC®ª 27853

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.

General Comments

(1) Refer to Table 1C 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.

(3) The susceptibility of *P. aeruginosa* isolated from patients with cystic fibrosis can be reliably determined by disk diffusion or dilution methods but may need extended incubation for up to 24 hours before reporting as susceptible.

(4) *P. aeruginosa* may develop resistance during prolonged therapy with all antimicrobial agents. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted.

(5) The dosage regimens shown in the comments column below are those necessary to achieve plasma drug exposures (in adults with normal renal and hepatic functions) on which breakpoints were derived. When implementing new breakpoints, it is strongly recommended that laboratories share this information with the antimicrobial stewardship team **and other relevant institutional stakeholders.**

"Warning": Do not report the following antimicrobial agents for bacteria isolated from CSF. These are not the drugs of choice and may not be effective for treating CSF infections caused by the bacteria included in Tables 2A through 2J:

- Agents administered by oral route only
- First- and second-generation cephalosporins and cephamycins
- Doripenem, ertapenem, and imipenem
- Clindamycin
- Lefamulin
- Macrolides
- Tetracyclines
- Fluoroquinolones

Refer to Glossary I for individual agents within the drug classes listed above.

Identification and Report of Resistant strains

- MRSA: Methicillin Resistant *Staphylococcus aureus*
- MR-CoNS: Methicillin Resistant Coagulase Negative *Staphylococci*
- VRSA: Vancomycin Resistant *Staphylococcus aureus*
- VISA: Vancomycin Intermediate *Staphylococcus aureus*
- VRE: Vancomycin Resistant *Enterococci*
- ESBL: Extended Spectrum Beta Lactamases-producing strains
- Carbapenemase-producing strains
- MDR: Multidrug-Resistant
- XDR: Extensively Drug-Resistant
- PDR: Pandrug-Resistant = TDR: Totally Drug-Resistant

MSSA vs. MRSA (2023)

Table 3G-1. Test for Detecting Methicillin (Oxacillin) Resistance in *Staphylococcus aureus*[a] and *Staphylococcus lugdunensis*

Test	Detecting *mecA*-Mediated Resistance Using Cefoxitin[b]		Detecting *mecA*-Mediated Resistance Using Oxacillin	Detecting *mecA*-mediated Resistance Using Oxacillin Salt Agar for *S. aureus* Only
Test method	Disk diffusion	Broth microdilution	Broth microdilution and agar dilution	Agar dilution for *S. aureus*
Medium	MHA	CAMHB	CAMHB with 2% NaCl (broth microdilution) MHA with 2% NaCl (agar dilution)	MHA with 4% NaCl
Antimicrobial concentration	30-µg cefoxitin disk	4 µg/mL cefoxitin	2 µg/mL oxacillin	6 µg/mL oxacillin
Inoculum	Standard disk diffusion procedure	Standard broth microdilution procedure	Standard broth microdilution procedure or standard agar dilution procedure	Colony suspension to obtain 0.5 McFarland turbidity Using a 1-µL loop that was dipped in the suspension, spot an area 10-15 mm in diameter. Alternatively, using a swab dipped in the suspension and the excess liquid expressed, spot a similar area or streak an entire quadrant.
Incubation conditions	33 to 35°C; ambient air[c]			
Incubation length	16-18 hours	16-20 hours	24 hours (may be reported after 18 hours, if resistant)	24 hours; read with transmitted light
Results	≤ 21 mm = positive for *mecA*-mediated resistance ≥ 22 mm = negative for *mecA*-mediated resistance	≥ 8 µg/mL = positive for *mecA*-mediated resistance ≤ 4 µg/mL = negative for *mecA*-mediated resistance	≥4 µg/mL = positive for *mecA*-mediated resistance ≤ 2 µg/mL = negative for *mecA*-mediated resistance	Examine carefully with transmitted light for > 1 colony or light film of growth. > 1 colony = positive for *mecA*-mediated resistance
Additional testing and reporting	Isolates that test positive for *mecA*-mediated resistance should be reported as methicillin (oxacillin) (not cefoxitin) resistant; other β-lactam agents, except ceftaroline, should be reported as resistant or should not be reported.[d]			
QC recommendations - routine[e,f]	*S. aureus* ATCC®[g] 25923 - *mecA* negative (zone 23-29 mm)	*S. aureus* ATCC® 29213 - *mecA* negative (MIC 1-4 µg/mL)	*S. aureus* ATCC® 29213 - *mecA* negative (MIC 0.12-0.5 µg/mL)	*S. aureus* ATCC®[c] 29213 - susceptible (≤ 1 colony; with each test day)
QC recommendations - lot/shipment[h]	N/A	*S. aureus* ATCC® 43300 - *mecA* positive (MIC ≥ 8 µg/mL)	*S. aureus* ATCC® 43300 - *mecA* positive (MIC ≥ 8 µg/mL)	*S. aureus* ATCC® 43300 - *mecA* positive (>1 colony)

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant *Staphylococcus* spp.; N/A, not applicable.

CoNS vs. MR-CoNS

Table 3G-2. Test for Detecting Methicillin (Oxacillin) Resistance in *Staphylococcus* spp. Except *Staphylococcus aureus*[a] and *Staphylococcus lugdunensis*

Test	Detecting *mecA*-Mediated Resistance Using Cefoxitin[b]	Detecting *mecA*-Mediated Resistance Using Oxacillin	
Test method	Disk diffusion	Disk diffusion	Broth microdilution and agar dilution
Organism group	*Staphylococcus* spp. except: *S. aureus* (refer to Table 3G-1) *S. lugdunensis* (refer to Table 3G-1) *S. pseudintermedius* (not recommended) *S. schleiferi* (not recommended)	Testing is only indicated for the species listed below: *S. epidermidis* *S. pseudintermedius* *S. schleiferi*	*Staphylococcus* spp. except: *S. aureus* (refer to Table 3G-1) *S. lugdunensis* (refer to Table 3G-1)
Medium	MHA	MHA	CAMHB with 2% NaCl (broth microdilution) MHA with 2% NaCl (agar dilution)
Antimicrobial concentration	30 µg cefoxitin disk	1-µg oxacillin disk	0.5 µg/mL oxacillin
Inoculum	Standard disk diffusion procedure	Standard disk diffusion procedure	Standard broth microdilution procedure or standard agar dilution procedure
Incubation conditions	33 to 35°C; ambient air[c]		
Incubation length	24 hours (may be reported after 18 hours, if resistant)	16-18 hours	24 hours (may be reported after 18 hours, if resistant)
Results	≤ 24 mm = positive for *mecA*-mediated resistance ≥ 25 mm = negative for *mecA*-mediated resistance	≤ 17 mm = positive for *mecA*-mediated resistance ≥ 18 mm = negative for *mecA*-mediated resistance	≥ 1 µg/mL = positive for *mecA*-mediated resistance ≤ 0.5 µg/mL = negative for *mecA*-mediated resistance
Additional testing and reporting	Isolates that test positive for *mecA*-mediated resistance should be reported as methicillin (oxacillin) (not cefoxitin) resistant; other β-lactam agents, except ceftaroline, should be reported as resistant or should not be reported.[d]		
			For *Staphylococcus* spp., excluding *S. aureus*, *S. lugdunensis*, *S. epidermidis*, *S. pseudintermedius*, and *S. schleiferi*, oxacillin MIC breakpoints may overcall resistance, and some isolates for which the oxacillin MICs are 1-2 µg/mL may be *mecA* negative. Isolates from serious infections for which oxacillin MICs are 1-2 µg/mL may be tested for *mecA* or for PBP2a. Isolates that test *mecA* or PBP2a negative should be reported as methicillin (oxacillin) susceptible.
QC recommendations - routine[e]	*S. aureus* ATCC® 25923 - *mecA* negative (zone 23-29 mm)	*S. aureus* ATCC® 25923 - *mecA* negative (zone 18-24 mm)	*S. aureus* ATCC® 29213 - *mecA* negative (MIC 0.12-0.5 µg/mL)
QC recommendations - lot/shipment[f]	N/A	*S. aureus* ATCC® 43300 - *mecA* positive (zone ≤ 24 mm)	*S. aureus* ATCC® 43300 - *mecA* positive (MIC ≥ 8 µg/mL)

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant *Staphylococcus* spp.; N/A, not applicable.

VRSA , VISA & VRE

Table 3H. Vancomycin Agar Screen for *Staphylococcus aureus* and *Enterococcus* spp.

Screen Test	Vancomycin MIC ≥ 8 µg/mL	
Test method	Agar dilution	Agar dilution
Organism group	*S. aureus*	*Enterococcus* spp.
Medium	BHI agar	BHI[a] agar
Antimicrobial concentration	6 µg/mL vancomycin	6 µg/mL vancomycin
Inoculum	Colony suspension to obtain 0.5 McFarland turbidity Preferably, using a micropipette, spot a 10-µL drop onto agar surface. Alternatively, using a swab dipped in the suspension and the excess liquid expressed, spot an area 10-15 mm in diameter or streak a portion of the plate.	1-10 µL of a 0.5 McFarland suspension spotted onto agar surface. Alternatively, using a swab dipped in the suspension and the excess liquid expressed, spot an area 10-15 mm in diameter or streak a portion of the plate.
Incubation conditions	35°C ± 2°C; ambient air	35°C ± 2°C; ambient air
Incubation length	24 hours	24 hours
Results	Examine carefully with transmitted light for > 1 colony or light film of growth. > 1 colony = presumptive reduced susceptibility to vancomycin	> 1 colony = presumptive vancomycin resistance
Additional testing and reporting	Perform a vancomycin MIC using a validated MIC method to determine vancomycin MICs on *S. aureus* that grow on BHI-vancomycin screening agar. Testing on BHI-vancomycin screening agar does not reliably detect all vancomycin-intermediate *S. aureus* strains. Some strains for which the vancomycin MICs are 4 µg/mL will fail to grow.	Perform vancomycin MIC on *Enterococcus* spp. that grow on BHI-vancomycin screening agar and test for motility and pigment production to distinguish species with acquired resistance (eg, *vanA* and *vanB*) from those with intrinsic, intermediate-level resistance to vancomycin (eg, *vanC*), such as *Enterococcus gallinarum* and *Enterococcus casseliflavus*, which often grow on the vancomycin screen plate. In contrast to other enterococci, *E. casseliflavus* and *E. gallinarum* with vancomycin MICs of 8-16 µg/mL (intermediate) differ from vancomycin-resistant enterococci for infection prevention purposes.
QC recommendations - routine[b]	*E. faecalis* ATCC®[c] 29212 - susceptible	*E. faecalis* ATCC® 29212 - susceptible
QC recommendations - lot/shipment[d]	*E. faecalis* ATCC® 51299 - resistant	*E. faecalis* ATCC® 51299 - resistant

Abbreviations: ATCC®, American Type Culture Collection; BHI, brain heart infusion; MIC, minimal inhibitory concentration; QC, quality control.

Table 2D. *Enterococcus* spp. (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	SDD	I	R	
PENICILLINS (Continued)									
Penicillin	10 units	≥15	-	≤14	≤8	-	-	≥16	**(12)** Penicillin or ampicillin resistance among enterococci due to β-lactamase production has been reported very rarely. Penicillin or ampicillin resistance due to β-lactamase production is not reliably detected with routine disk or dilution methods but is detected using a direct, nitrocefin-based β-lactamase test. Because of the rarity of β-lactamase-positive enterococci, this test does not need to be performed routinely but can be used in selected cases. A positive β-lactamase test predicts resistance to penicillin as well as amino- and ureidopenicillins (see Glossary I).
Ampicillin	10 µg	≥17	-	≤16	≤8	-	-	≥16	
GLYCOPEPTIDES									
Vancomycin	30 µg	≥17	15-16	≤14	≤4	-	8-16	≥32	**(13)** When testing vancomycin against enterococci, plates should be held a full 24 hours for accurate detection of resistance. Zones should be examined using transmitted light; the presence of a haze or any growth within the zone of inhibition indicates resistance. Organisms with intermediate zones should be tested by an MIC method as described in M07.[3] For isolates for which the vancomycin MICs are 8-16 µg/mL, perform biochemical tests for identification as listed under the "Vancomycin MIC ≥ 8 µg/mL" test found in Table 3H. See general comment (5) and comment (9).

ESBL producing-Strains:

- Resistance to most beta-lactam antibiotics including:
  - ✓ Penicillins
  - ✓ Cephalosporins
  - ✓ Monobactam aztreonam

ESBL Test

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*: 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.	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).
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.	

Table 3A. (Continued)

Test	Criteria for Performance of ESBL Test		ESBL Test	
Test method	Disk diffusion	Broth microdilution	Disk diffusion	Broth microdilution
QC recommendations	When testing antimicrobial agents used for ESBL detection, *K. pneumoniae* ATCC®[b] 700603 is provided as a supplemental QC strain (eg, for training, competence assessment, or test evaluation). Either strain, *K. pneumoniae* ATCC® 700603 or *E. coli* ATCC® 25922, may then be used for routine QC (eg, weekly or daily).	When testing antimicrobial agents used for ESBL detection, *K. pneumoniae* ATCC® 700603 is provided as a supplemental QC strain (eg, for training, competence assessment, or test evaluation). Either strain, *K. pneumoniae* ATCC® 700603 or *E. coli* ATCC® 25922, may then be used for routine QC (eg, weekly or daily).	When performing the ESBL test, *K. pneumoniae* ATCC® 700603 and *E. coli* ATCC® 25922 should be used for routine QC (eg, weekly or daily).	When performing the ESBL test, *K. pneumoniae* ATCC® 700603 and *E. coli* ATCC® 25922 should be tested routinely (eg, weekly or daily).
	E. coli ATCC® 25922 (see acceptable QC ranges in Table 4A-1)	*E. coli* ATCC® 25922 = no growth (see acceptable QC ranges listed in Table 5A-1)	**Acceptable QC:** *E. coli* ATCC® 25922: ≤ 2-mm increase in zone diameter for antimicrobial agent tested in combination with clavulanate vs the zone diameter when tested alone.	**Acceptable QC:** *E. coli* ATCC® 25922: < 3 2-fold concentration decrease in MIC for antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone.
	K. pneumoniae ATCC® 700603: Cefpodoxime zone 9-16 mm Ceftazidime zone 10-18 mm Aztreonam zone 10-16 mm Cefotaxime zone 17-25 mm Ceftriaxone zone 16-24 mm	*K. pneumoniae* ATCC® 700603 = Growth: Cefpodoxime MIC ≥8 µg/mL Ceftazidime MIC ≥2 µg/mL Aztreonam MIC ≥2 µg/mL Cefotaxime MIC ≥2 µg/mL Ceftriaxone MIC ≥2 µg/mL	*K. pneumoniae* ATCC® 700603: ≥ 5-mm increase in zone diameter of ceftazidime-clavulanate vs ceftazidime alone; ≥ 3-mm increase in zone diameter of cefotaxime-clavulanate vs cefotaxime alone.	*K. pneumoniae* ATCC® 700603: ≥3 2-fold concentration decrease in MIC for an antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone.

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; ESBL, extended-spectrum β-lactamase; **FDA, US Food and Drug Administration;** MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; PK/PD, pharmacokinetic/pharmacodynamic; QC, quality control.

CBDE, CAT

Test	Colistin Broth Disk Elution	Colistin Agar Test
Approved organisms	Enterobacterales and *Pseudomonas aeruginosa*	Enterobacterales and *P. aeruginosa*
Strengths	No special reagents or media necessary	Ability to test up to 10 isolates at one time
Limitations	Hands-on time and cost	Requires special media (colistin agar plate)
When to perform this test	Testing multidrug-resistant isolates for clinical or infection prevention purposes	Testing multidrug-resistant isolates for clinical or infection prevention purposes
Test method	Tube dilution using colistin disk as the colistin source	Agar dilution: slight variation of method described in M07[2] (ie, different inoculum and different approach to interpreting results)
Organism group	Enterobacterales and *P. aeruginosa*	Enterobacterales and *P. aeruginosa*
Medium	CAMHB (10-mL tubes)	MHA (20 mL in 100-mm Petri plate)[a]
Antimicrobial concentration	10-µg colistin sulfate disks Final concentration: 0 µg/mL (growth control), 1 µg/mL, 2 µg/mL, and 4 µg/mL colistin	Colistin sulfate Final concentration: 0 µg/mL (growth control), 1 µg/mL, 2 µg/mL, and 4 µg/mL colistin[a]
Inoculum	1. Using a loop or swab, pick 3-5 colonies from a fresh (18-24 hours) nonselective agar plate and transfer to sterile saline (4-5 mL). 2. Adjust turbidity to equivalent of a 0.5 McFarland turbidity standard.	1. Using a loop or swab, pick 3-5 colonies from a fresh (18-24 hours) nonselective agar plate and transfer to sterile saline (4-5 mL). 2. Adjust turbidity to equivalent of a 0.5 McFarland turbidity standard. 3. Dilute the standardized inoculum 1:10 in saline.

Inducible Clindamycin (D-Zone) Test

Table 3I. Tests for Detecting Inducible Clindamycin Resistance in *Staphylococcus* spp., *Streptococcus pneumoniae*, and *Streptococcus* spp. ß-Hemolytic Group[a,b]

Test	ICR			
Test method	Disk Diffusion (D-zone test)		Broth Microdilution	
Organism group (applies only to organisms resistant to erythromycin and susceptible or intermediate to clindamycin)	All *Staphylococcus* spp.	*S. pneumoniae* and ß-hemolytic *Streptococcus* spp.	All *Staphylococcus* spp.[c]	*S. pneumoniae* and ß-hemolytic *Streptococcus* spp.
Medium	MHA or blood agar purity plate used with MIC tests	MHA supplemented with sheep blood (5% v/v) or TSA supplemented with sheep blood (5% v/v)	CAMHB	CAMHB with LHB (2.5% to 5% v/v)
Antimicrobial concentration	15-µg erythromycin and 2-µg clindamycin disks spaced 15-26 mm apart	15-µg erythromycin and 2-µg clindamycin disks spaced 12 mm apart	4 µg/mL erythromycin and 0.5 µg/mL clindamycin in same well	1 µg/mL erythromycin and 0.5 µg/mL clindamycin in same well
Inoculum	Standard disk diffusion procedure or heavily inoculated area of purity plate	Standard disk diffusion procedure	Standard broth microdilution procedure	
Incubation conditions	35°C ± 2°C; ambient air	35°C ± 2°C; 5% CO_2	35°C ± 2°C; ambient air	
Incubation length	16-18 hours	20-24 hours	18-24 hours	20-24 hours
Results	Flattening of the zone of inhibition adjacent to the erythromycin disk (referred to as a D-zone) = ICR. Hazy growth within the zone of inhibition around clindamycin = clindamycin resistance, even if no D-zone is apparent.		Any growth = ICR. No growth = no ICR.	

ORIGINAL ARTICLE BACTERIOLOGY

Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance

A.-P. Magiorakos[1], A. Srinivasan[2], R. B. Carey[2], Y. Carmeli[3], M. E. Falagas[4,5], C. G. Giske[6], S. Harbarth[7], J. F. Hindler[8], G. Kahlmeter[9], B. Olsson-Liljequist[10], D. L. Paterson[11], L. B. Rice[12], J. Stelling[13], M. J. Struelens[1], A. Vatopoulos[14], J. T. Weber[2] and D. L. Monnet[1]

1) European Centre for Disease Prevention and Control, Stockholm, Sweden, 2) Office of Infectious Diseases, Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, GA, USA, 3) Division of Epidemiology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, 4) Alfa Institute of Biomedical Sciences (AIBS), Athens, Greece, 5) Department of Medicine, Tufts University School of Medicine, Boston, MA, USA, 6) Department of Clinical Microbiology, Karolinska University Hospital, Stockholm, Sweden, 7) Infection Control Programme, University of Geneva Hospitals, Geneva, Switzerland, 8) Department of Pathology and Laboratory Medicine, University of California Los Angeles Medical Center, Los Angeles, CA, USA, 9) Department of Clinical Microbiology, Central Hospital, Växjö, 10) Department of Bacteriology, Swedish Institute for Infectious Disease Control, Solna, Sweden, 11) The University of Queensland Centre for Clinical Research, Royal Brisbane and Women's Hospital, Brisbane, Qld, Australia, 12) Warren Alpert Medical School of Brown University, Providence, RI, 13) Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA and 14) Department of Microbiology, National School of Public Health, Athens, Greece

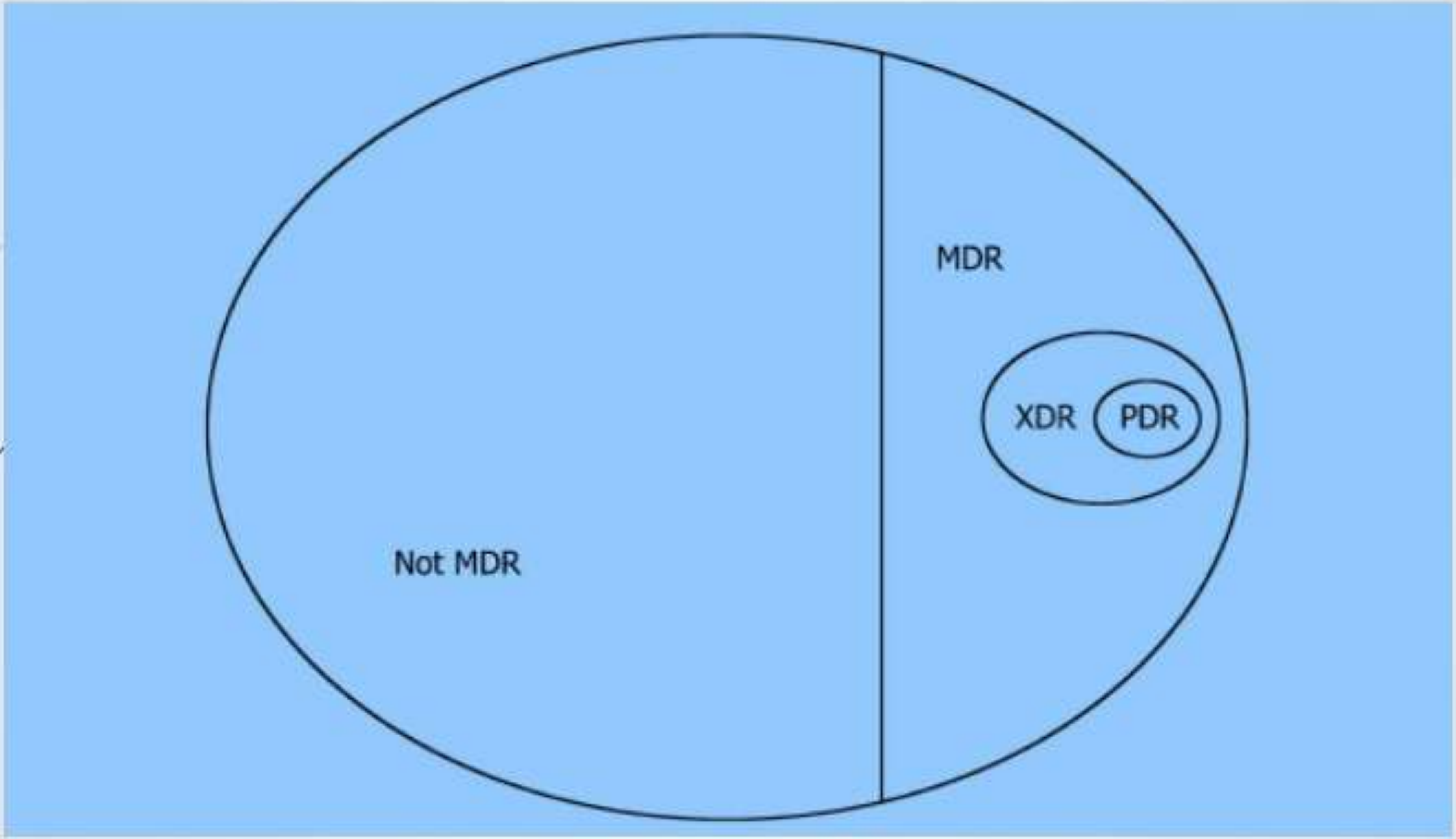

MDR
XDR
PDR
Not MDR

TABLE 6. Definitions for multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant (PDR) bacteria

Bacterium	MDR	XDR	PDR
Staphylococcus aureus	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories listed in Table 1[a]	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 1.	Non-susceptibility to all agents in all antimicrobial categories for each bacterium in Tables 1–5
Enterococcus spp.	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories listed in Table 2	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 2.	
Enterobacteriaceae	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories listed in Table 3	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 3.	
Pseudomonas aeruginosa	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories listed in Table 4	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 4.	
Acinetobacter spp.	The isolate is non-susceptible to at least 1 agent in ≥3 antimicrobial categories listed in Table 5	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 5.	

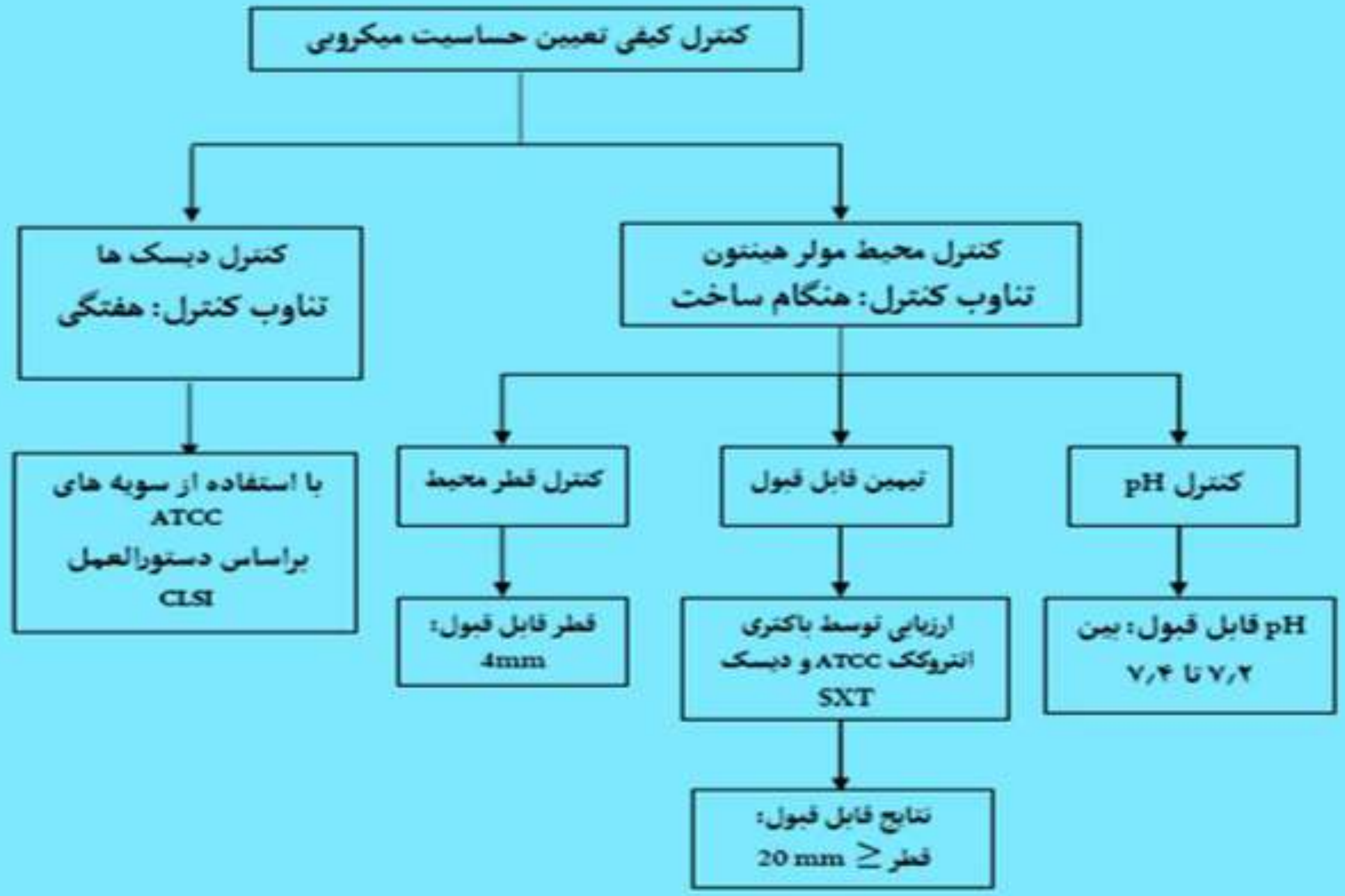
[a]All MRSA isolates are defined as MDR because resistance to oxacillin or cefoxitin predicts non-susceptibility to all categories of β-lactam antimicrobials listed in this document, with the exception of the anti-MRSA cephalosporins (i.e. all categories of penicillins, cephalosporins, β-lactamase inhibitors and carbapenems currently approved up until 25 January 2011).
http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/ARHAI/Pages/public_consultation_clinical_microbiology_infection_article.aspx.

TABLE 7. ***Pseudomonas aeruginosa*; examples of antimicrobial susceptibility profiles that fit MDR, XDR and PDR definitions; isolate no. 1 is PDR; isolate no. 2 is XDR and isolate no. 3 is MDR**

Antimicrobial category	Antimicrobial agent	Isolate no. 1 (PDR)	Isolate no. 2 (XDR)	Isolate no. 3 (MDR)
Aminoglycosides	Gentamicin	X[a]	X	
	Tobramycin	X	[b]	
	Amikacin	X		
	Netilmicin	X		
Antipseudomonal carbapenems	Imipenem	X	X	X
	Meropenem	X	X	
	Doripenem	X	X	
Antipseudomonal cephalosporins	Ceftazidime	X		X
	Cefepime	X	X	
Antipseudomonal fluoroquinolones	Ciprofloxacin	X	X	X
	Levofloxacin	X		
Antipseudomonal penicillins + β-lactamase inhibitors	Piperacillin-tazobactam	X		
	Ticarcillin-clavulanic acid	X	X	
Monobactams	Aztreonam	X	X	
Phosphonic acids	Fosfomycin	X		
Polymyxins	Colistin	X		
	Polymyxin B	X		

	• ادامه آزمایش تعیین حساسیت ضدمیکروبی (آنتی بیوگرام)	سنجه	حداکثر امتیاز هر سنجه	حداکثر امتیاز هر سؤال	امتیاز کسب شده	کاربرد ندارد	توضیحات
۴۸	آیا در آزمایشگاه، عفونت های مقاوم ناشی از باکتری های MDR (Multidrug resistant)، XDR (Extensively drug resistant) و PDR (Pandrug resistant) به پزشک معالج و پرستار یا پزشک کنترل عفونت به عنوان نتیجه بحرانی و نیز به صورت دوره ای گزارش می شود؟ توجه: (اگر آزمایشگاه عفونت های مقاوم ناشی از هر کدام از باکتری های MDR، XDR، PDR را گزارش کند، امتیاز سنجه اول را به طور کامل می گیرد. ضمناً آزمایشگاه یا امتیاز سنجه گزارش توسط نرم افزار را می گیرد، یا امتیاز سنجه گزارش دستی را، بنابراین حداکثر امتیاز این سؤال، ۵ می باشد).	آگاهی کارکنان و گزارش موارد زیر: MDR: باکتری هایی که حداقل به سه آنتی بیوتیک از سه کلاس مختلف مقاوم باشند. XDR: باکتری هایی که تنها به یک یا دو آنتی بیوتیک از کلاس های مختلف حساس باشند. PDR: باکتری هایی که به تمامی آنتی بیوتیک های مورد آزمایش مقاوم باشند.	۱	۵			
		گزارش توسط نرم افزار WHONET 5.6	۲				
		گزارش دستی (غیر از نرم افزار WHONET)	۱				
		وجود سوابق گزارش فوری یا دوره ای و صحت سوابق	۲				

QA & QC in AST:


کنترل کیفی تعیین حساسیت میکروبی
کنترل دیسک ها
تناوب کنترل: هفتگی
کنترل محیط مولر هینتون
تناوب کنترل: هنگام ساخت
با استفاده از سویه های ATCC
براساس دستورالعمل CLSI
کنترل قطر محیط
تعیین قابل قبول
کنترل pH
قطر قابل قبول: 4mm
ارزیابی توسط باکتری انتروکک ATCC و دیسک SXT
pH قابل قبول: بین ۷،۲ تا ۷،۴
نتایج قابل قبول:
قطر ≥ 20 mm

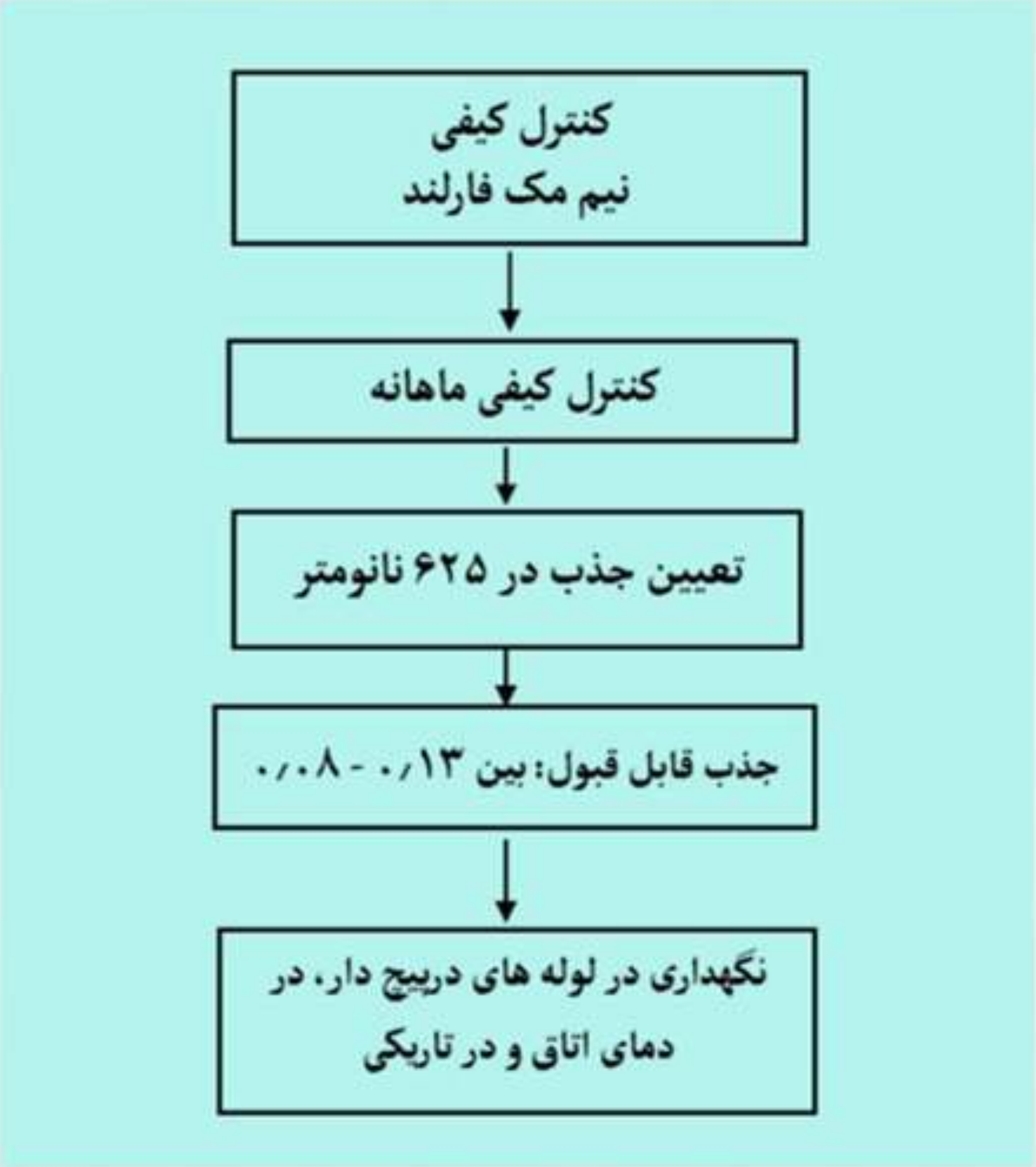

کنترل کیفی
نیم مک فارلند
کنترل کیفی ماهانه
تعیین جذب در ۶۲۵ نانومتر
جذب قابل قبول: بین ۰٫۱۳ - ۰٫۰۸
نگهداری در لوله های درپیچ دار، در
دمای اتاق و در تاریکی

Table 4C. Disk Diffusion Reference Guide to QC Frequency

This table summarizes the suggested QC frequency when modifications are made to antimicrobial susceptibility test systems (refer to CLSI document EP23[™1]). It applies only to antimicrobial agents for which satisfactory results have been obtained with either the 15-replicate (3- × 5-day) plan or 20 or 30 consecutive test day plan. Otherwise QC is required each test day.

Test Modification	Recommended QC Frequency: 1 Day	Recommended QC Frequency: 5 Days	Recommended QC Frequency: 15-Replicate Plan or 20- or 30-Day Plan	Comments
Disks				
Use new shipment or lot number.	X			
Use new manufacturer.	X			
Addition of new antimicrobial agent to existing system.			X	In addition, perform in-house verification studies.
Media (prepared agar plates)				
Use new shipment or lot number.	X			
Use new manufacturer.		X		
Inoculum preparation				
Convert inoculum preparation/ standardization to use of a device that has its own QC protocol.		X		**Example:** Convert from visual adjustment of turbidity to use of a photometric device for which a QC procedure is provided.
Convert inoculum preparation/ standardization to a method that depends on user technique.			X	**Example:** Convert from visual adjustment of turbidity to another method that is not based on a photometric device.
Measuring zones				
Change method of measuring zones.			X	**Example:** Convert from manual zone measurements to automated zone reader. In addition, perform in-house verification studies.
Instrument/software (eg, automated zone reader)				
Software update that affects AST results		X		Monitor all drugs, not just those implicated in software modification.
Repair of instrument that affects AST results	X			Depending on extent of repair (eg, critical component such as the photographic device), additional testing may be appropriate (eg, 5 days).

Abbreviations: AST, antimicrobial susceptibility testing; QC, quality control.

Table 4A-1. Disk Diffusion QC Ranges for Nonfastidious Organisms and Antimicrobial Agents Excluding β-Lactam Combination Agents[a]

Antimicrobial Agent	Disk Content	Disk Diffusion QC Ranges, mm		
		Escherichia coli ATCC® 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 25923
Amikacin	30 µg	19-26	20-26	20-26
Ampicillin	10 µg	15-22	-	27-35
Azithromycin	15 µg	-	-	21-26
Azlocillin	75 µg	-	24-30	-
Aztreonam	30 µg	28-36	23-29	-
Carbenicillin	100 µg	23-29	18-24	-
Cefaclor	30 µg	23-27	-	27-31
Cefamandole	30 µg	26-32	-	26-34
Cefazolin	30 µg	21-27	-	29-35
Cefdinir	5 µg	24-28	-	25-32
Cefditoren	5 µg	22-28	-	20-28
Cefepime	30 µg	31-37	25-31	23-29
Cefetamet	10 µg	24-29	-	-
Cefiderocol	30 µg	25-31	22-31	-
Cefixime	5 µg	20-26	-	-
Cefmetazole	30 µg	26-32	-	25-34
Cefonicid	30 µg	25-29	-	22-28
Cefoperazone	75 µg	28-34	23-29	24-33
Cefotaxime	30 µg	29-35	18-22	25-31
Cefotetan	30 µg	28-34	-	17-23
Cefoxitin	30 µg	23-29	-	23-29
Cefpodoxime	10 µg	23-28	-	19-25
Cefprozil	30 µg	21-27	-	27-33
Ceftaroline	30 µg	26-34	-	26-35
Ceftazidime	30 µg	25-32	22-29	16-20
Ceftibuten	30 µg	27-35	-	-
Ceftizoxime	30 µg	30-36	12-17	27-35
Ceftobiprole	5 µg	25-31	-	20-27
Ceftriaxone	30 µg	29-35	17-23	22-28
Cefuroxime	30 µg	20-26	-	27-35
Cephalothin	30 µg	15-21	-	29-37
Chloramphenicol	30 µg	21-27	-	19-26
Cinoxacin	100 µg	26-32	-	-

Aminoglycosides Quinolones	Any	Zone too small	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
	Any	Zone too large	pH of media too high	Acceptable pH range = 7.2–7.4
Aminoglycosides	*P. aeruginosa* ATCC® 27853	Zone too small	Ca++ and/or Mg++ content too high	Use alternative lot of media.
Aminoglycosides	*P. aeruginosa* ATCC® 27853	Zone too large	Ca++ and/or Mg++ content too low	Use alternative lot of media.
Clindamycin Macrolides	*S. aureus* ATCC® 25923	Zone too small	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
	S. aureus ATCC® 25923	Zone too large	pH of media too high	Acceptable pH range = 7.2–7.4
Quinolones	Any	Zone too small	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Quinolones	Any	Zone too large	pH of media too high	Acceptable pH range = 7.2–7.4
Tetracyclines	Any	Zone too large	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Tetracyclines	Any	Zone too small	pH of media too high	Acceptable pH range = 7.2–7.4
Tetracyclines	Any	Zone too small	Ca++ and/or Mg++ content too high	Use alternative lot of media.
Tetracyclines	Any	Zone too large	Ca++ and/or Mg++ content too low	Use alternative lot of media.
Sulfonamides Trimethoprim Trimethoprim-sulfamethoxazole	*E. faecalis* ATCC® 29212	Zone ≤ 20 mm	Media too high in thymidine content	Use alternative lot of media.
ALL AGENTS				
Various	Various	Zone too small	Contamination Use of magnification to read zones	Measure zone edge with visible growth detected with unaided eye. Subculture to determine purity and repeat if necessary.
Various	Any	Inoculum too light Error in inoculum preparation Media depth too thin MHA nutritionally unacceptable	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Use agar with depth approximately 4 mm. Recheck alternate lots of MHA.	
Various	Any	Many zones too small	Inoculum too heavy Error in inoculum preparation Media depth too thick	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Use agar with depth approximately 4 mm. Recheck alternate lots of MHA.

WHONET 2022 software

- The microbiology laboratory database software
- WHO Collaborating Centre for Surveillance of Antimicrobial Resistance
- Supporting Global Surveillance of Infectious Diseases
- Automated Outbreak Detection Software, Services, and Full Support
- CLSI , EUCAST breakpoint

www.whonet.org

Microbiology Critical Value

Microbiology Critical Values	
Test	**Critical Value Notification**
Blood Culture	Positive Smear Or Culture
CerebrocSpinal Fluid(CSF) Exam	Positive Smear Or Culture
Acid Fast Bacili – AFB	Positive Smear Or Culture
Herpes Culture	Positive Culture From Female Genital Specimen
Genital Culture	Positive Culture For Neisseria Gonorrhoeae And GroupB Strep From Inpatient /OB Genital , Placenta
Cryptococal Antigens	Positive
Hepatitis Surface Antigen	Positive Poostpartum Within 24 hrs
Positive Tissue Cultures (Liver,Bine Biopsies,ets.)	
Beta – Hemolytic Streptococci,Group A From Sterile Sites	
Neisseria Gonorrhoeae From Eyes	
Clostridium Botulinum, Clostridium Perfringenes, Clostridium Tetanus	
Coryneacterium Diphteriae	
Legionella Species	
Listeria Species	
Positive Modified Acid Fast And Ziehl- Neelsen Stains	
Unusually Resistant Organisms Including: ***Vancomycin Resistant Entrococci (VRE)** ***Methicilin Resistant Staphylococcus Aureus (MRSA)** ***Multiply Resistant Gram Negatve Or Any Other Highly Resistant Organism Or Organism With Unusual Susceptibility Pattern.On Blood/Sterile Fluids/Wound/ANO2/Screening Swabs,BAL,Tracheal Aspirates** ***Extended Spectrum Beta Lactamases (ESBLs)** ***Glycopeptide Intermediate StaphylococcusAureus (GISA) Borderline Oxacilin Resistant**	


Thanks for your attention