Principles and methods of antimicrobial susceptibility testing

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Cleveland Clinic

Today’s objective

Apply the principles of antimicrobial susceptibility testing (AST) and bacterial resistance mechanisms to the testing and interpretation of bacterial isolates.

- Compare various AST principles and procedures by definition and methodology.
- Define terms related to interpretation of susceptibility tests
- Explain the use of the McFarland turbidity standard when preparing an inoculum for AST.
- Describe the standard quality control documents for performing antimicrobial susceptibility testing.
- Describe AST based on dilution methods.
- Describe disk diffusion testing (Kirby-Bauer test) parameters and troubleshooting issues.
- Describe the gradient diffusion test (Epsilometer test “Etest”).
- Distinguish the principles of antimicrobial mechanisms of resistance.

Assumptions

- *in vitro* testing is useful
- *in vitro* testing predicts *in vivo* efficacy
- Interpretive criteria are appropriate
- *in vitro* testing is performed accurately:
  - Standard inoculum
  - Standard medium
  - Standard reagent drug concentration
  - Standard incubation time
- The mechanisms of resistance harbored by a microbe's neighbor does not directly impact the microbe's survival.
- Biology can be complex, and we do not understand everything that we observe.

Disclaimer

This lecture is not exhaustive.

This lecture is focused on antibacterials and does not discuss antifungal, antiparasitic, and antiviral drugs.

Most of the discussion will be based on the biology of microbes and not on how the microbes interact with humans, which is the end game.

Discussion will focus on antibiotic resistance and not resistance to other biocides.

Jargon to know

Prophylaxis
Antibiotics used to try to prevent an infection

Empiric therapy
Antibiotic(s) used when an infection is suspected or identified but when the pathogen or AST is not yet elucidated

Adequate therapy
Effective therapeutic regimen for treating a specific infection

Optimal therapy
Preferred therapeutic regimen for treating a specific infection; typically more targeted than empiric or adequate therapy

PK / PD

Pharmacokinetics

“What the body does to the antibiotic”

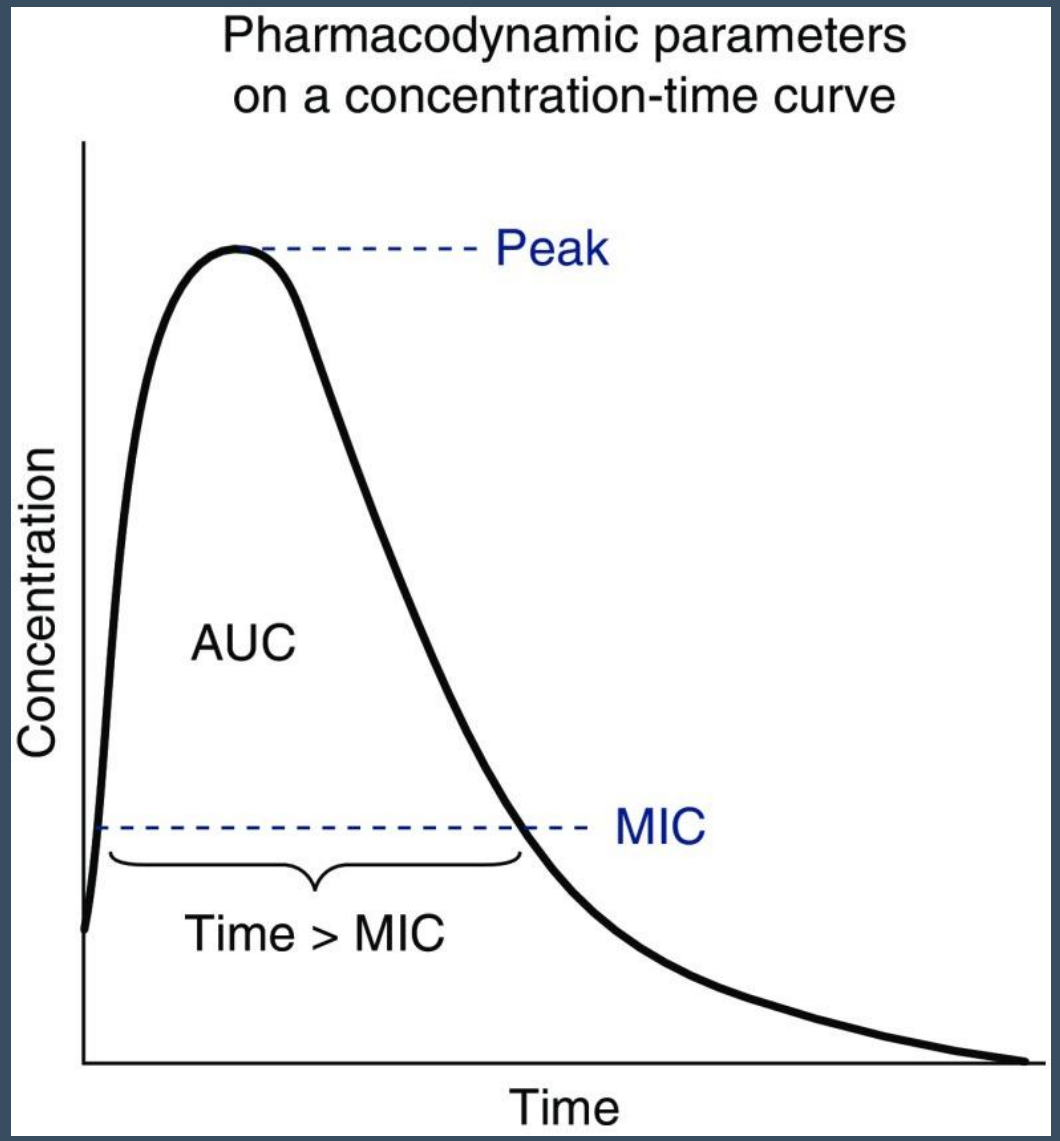
- How well is it absorbed by the body?
- How fast is it metabolized or excreted?
- Where does it concentrate?
- How much “free” antibiotic (not protein-bound) is available?

Pharmacodynamics

“What the antibiotic does to the bacteria”

- How long and at what concentration is needed to impact the bacteria’s metabolism?
- Bacteriostatic vs bactericidal

PK / PD



Pharmacodynamics of common antibiotic classes (5,6)

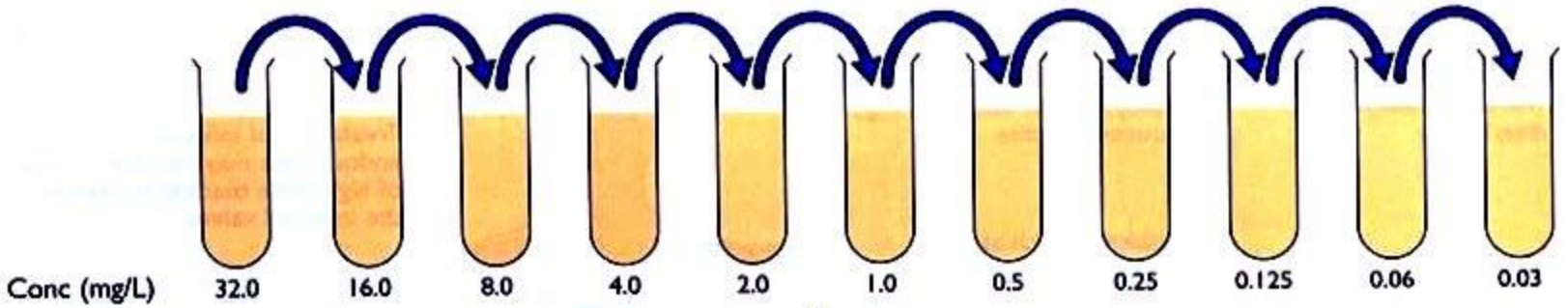
Antibiotic Class	Pharmacodynamic Profile	Pharmacodynamic Parameter to Optimize
Aminoglycosides	Concentration-dependent	Peak:MIC
Penicillins	Time-dependent	Time>MIC
Cephalosporins	Time-dependent	Time>MIC
Carbapenems	Time-dependent	Time>MIC
Vancomycin	Time-dependent	AUC:MIC
Lipopeptides	Concentration-dependent	AUC:MIC; peak:MIC
Oxazolidinones	Time-dependent	AUC:MIC
Lipoglycopeptides	Concentration-dependent	AUC:MIC
Fluoroquinolones	Concentration dependent	AUC:MIC
Macrolides	Time-dependent	AUC:MIC
Sulfamethoxazole-trimethoprim	Limited data (65)	Limited data (65)

Peak:MIC, maximum concentration (peak)-to-minimum inhibitory concentration ratio; Time>MIC, percentage of the dosing interval that concentrations stay above the minimum inhibitory concentration; AUC:MIC, drug exposure (area under the curve)-to-minimum inhibitory concentration ratio.

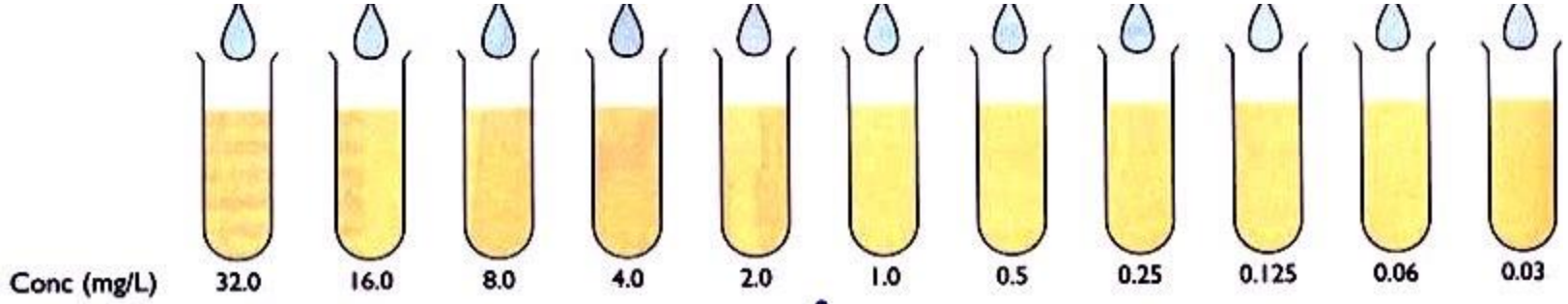
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6625637/

What is AST?

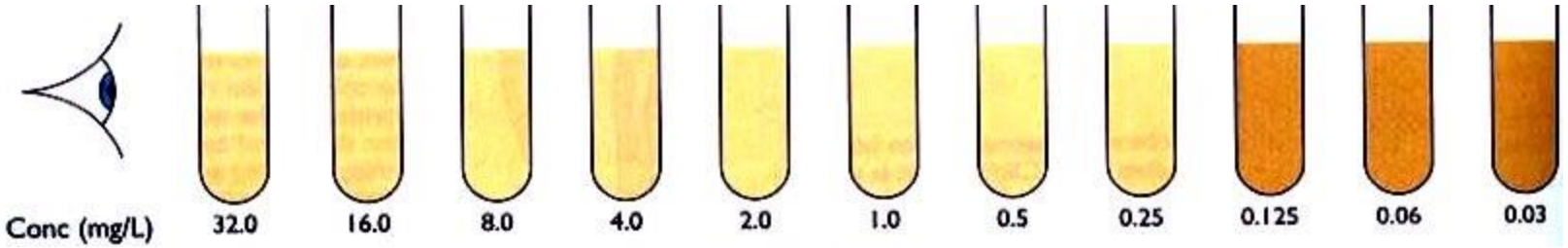
Doubling dilutions made in nutrient broth



Add ~10,000 cfu/mL of bacteria



Visually interpret growth after 18-24h of incubation at 35°C



Minimum inhibitory concentration (MIC) is 0.25 µg/ml

AST reference methods

Minimum inhibitory concentration (MIC) methods

Broth microdilution (BMD)

Can be performed in 100µl of broth in a 96-well plate

Broth macrodilution

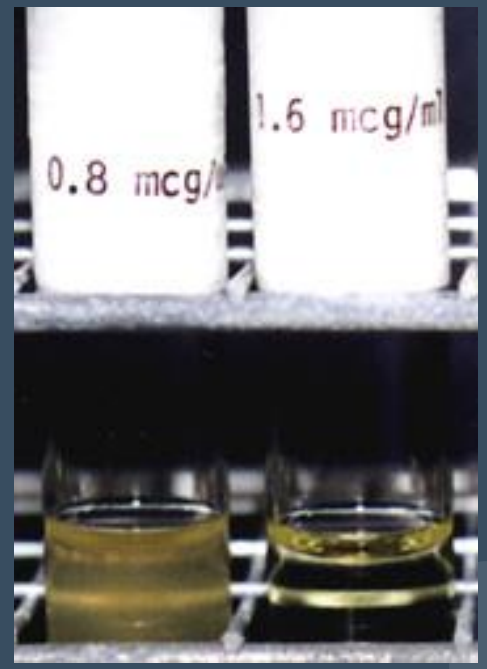
Performed in 1 mL of broth in glass tubes. Rarely used.

Agar dilution

Each plate has a different concentration of antibiotic, and multiple isolates can be tested using each plate. Rarely used (except at Mayo).

AST reference methods

Macrobroth dilution (MIC)

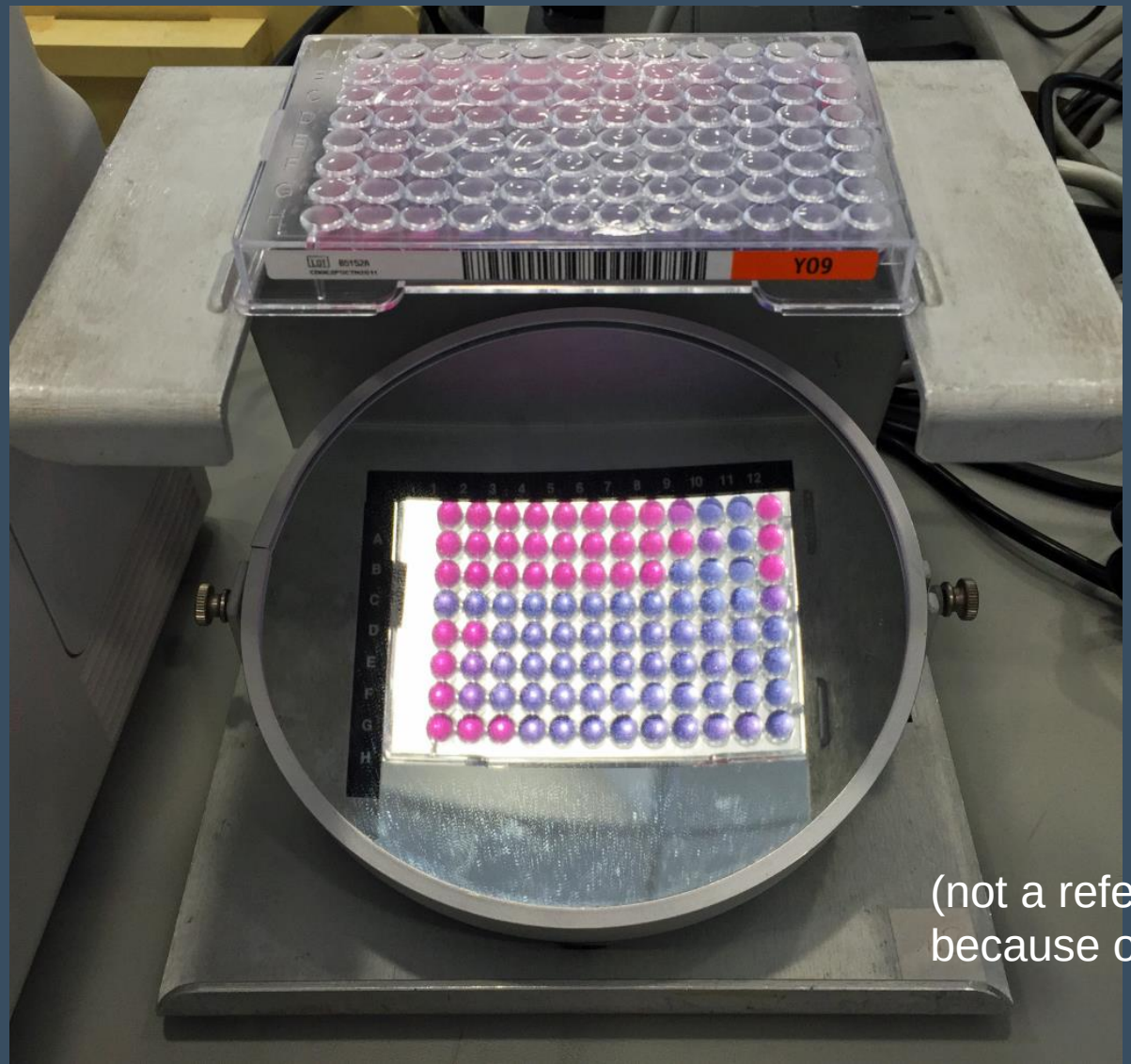


AST reference methods

Microbroth dilution (MIC)

AST reference methods

Microbroth dilution with resazurin/resorufin indicator



(not a reference method
because of the indicator dye)

AST reference methods

Agar dilution (MIC)

https://doi.org/10.1007/978-1-0716-0791-6_16

AST reference methods

Disk diffusion method

Disk diffusion testing

Disk diffusion is commonly referred to as “Kirby-Bauer” testing. Disk diffusion results are correlated to MIC results to determine breakpoints (see next slide).

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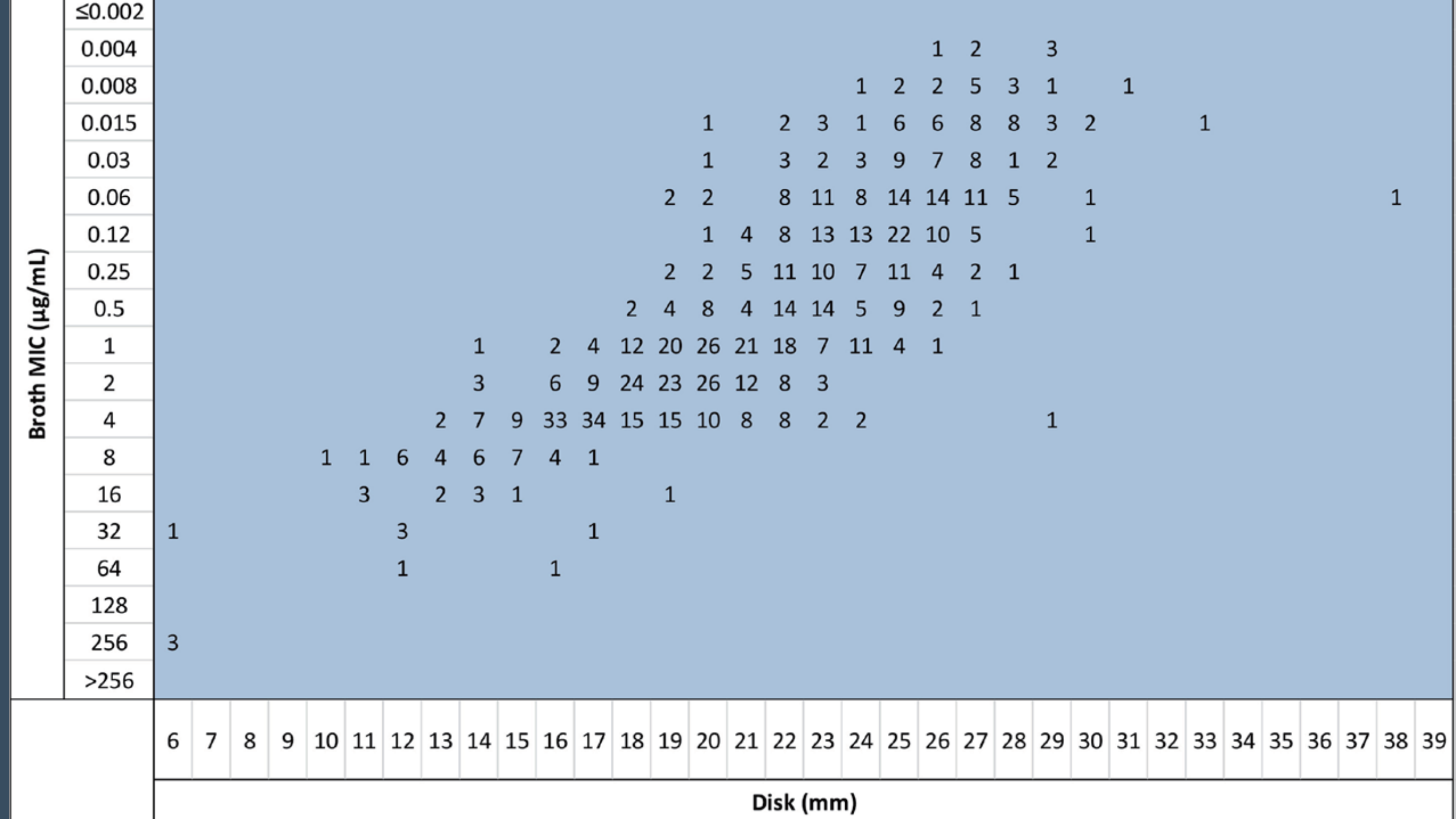
Vol. 36, No. 3, 1966

TECHNICAL SECTION

ANTIBIOTIC SUSCEPTIBILITY TESTING BY A STANDARDIZED SINGLE DISK METHOD

A. W. BAUER, M.D., W. M. M. KIRBY, M.D., J. C. SHERRIS, M.D., AND M. TURCK, M.D.

Departments of Microbiology and Medicine, University of Washington, School of Medicine, Seattle, Washington 98105


Broth MIC (µg/mL)
≤0.002
0.004
0.008
0.015
0.03
0.06
0.12
0.25
0.5
1
2
4
8
16
32
64
128
256
>256
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39
Disk (mm)

Broth MIC (µg/mL)	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
≤0.002																																		
0.004																					1	2		3										
0.008																			1	2	2	5	3	1		1								
0.015															1		2	3	1	6	6	8	8	3	2			1						
0.03															1		3	2	3	9	7	8	1	2										
0.06														2	2		8	11	8	14	14	11	5		1									1
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0.25														2	2	5	11	10	7	11	4	2	1											
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Disk (mm)

Broth MIC (µg/mL)	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
≤0.002																																		
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0.03															1		3	2	3	9	7	8	1	2										
0.06														2	2		8	11	8	14	14	11	5		1									1
0.12															1	4	8	13	13	22	10	5			1									
0.25														2	2	5	11	10	7	11	4	2	1											
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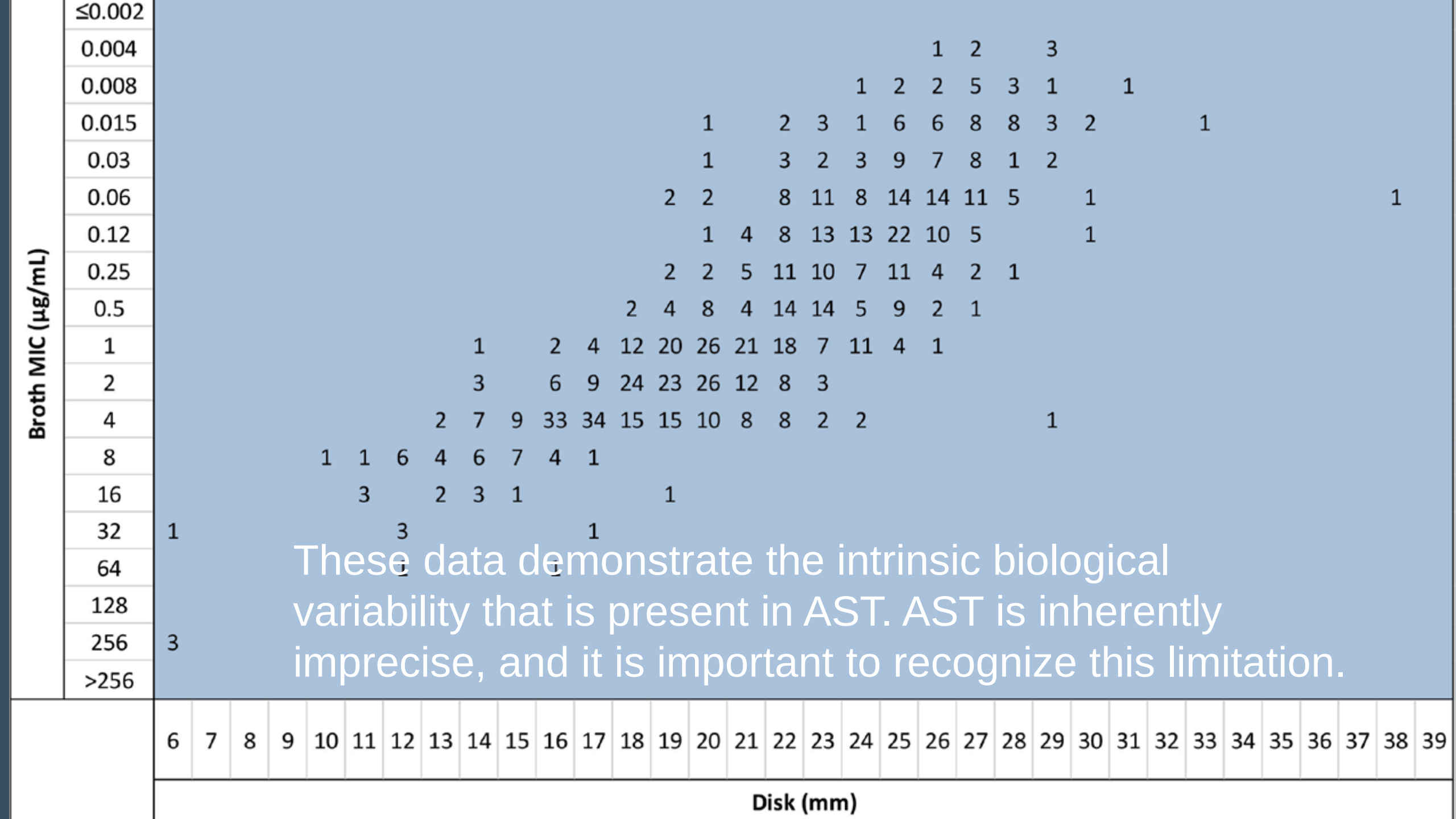
Disk (mm)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4
8
16
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6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39
Disk (mm)
These data demonstrate the intrinsic biological variability that is present in AST. AST is inherently imprecise, and it is important to recognize this limitation.

AST breakpoints

The “breakpoint” is where we choose to draw the line between “susceptible” and “resistant.”

The breakpoint is different for different antibiotics because the amount of drug that can be tolerated by a person (i.e. toxicity) and the amount of drug needed to inhibit microbial growth (i.e. potency) and the amount of protein binding (i.e. free drug & *in vivo* concentration duration) is different for each antibiotic.

AST breakpoints

The “breakpoint” is where we choose to draw the line between “susceptible” and “resistant.”

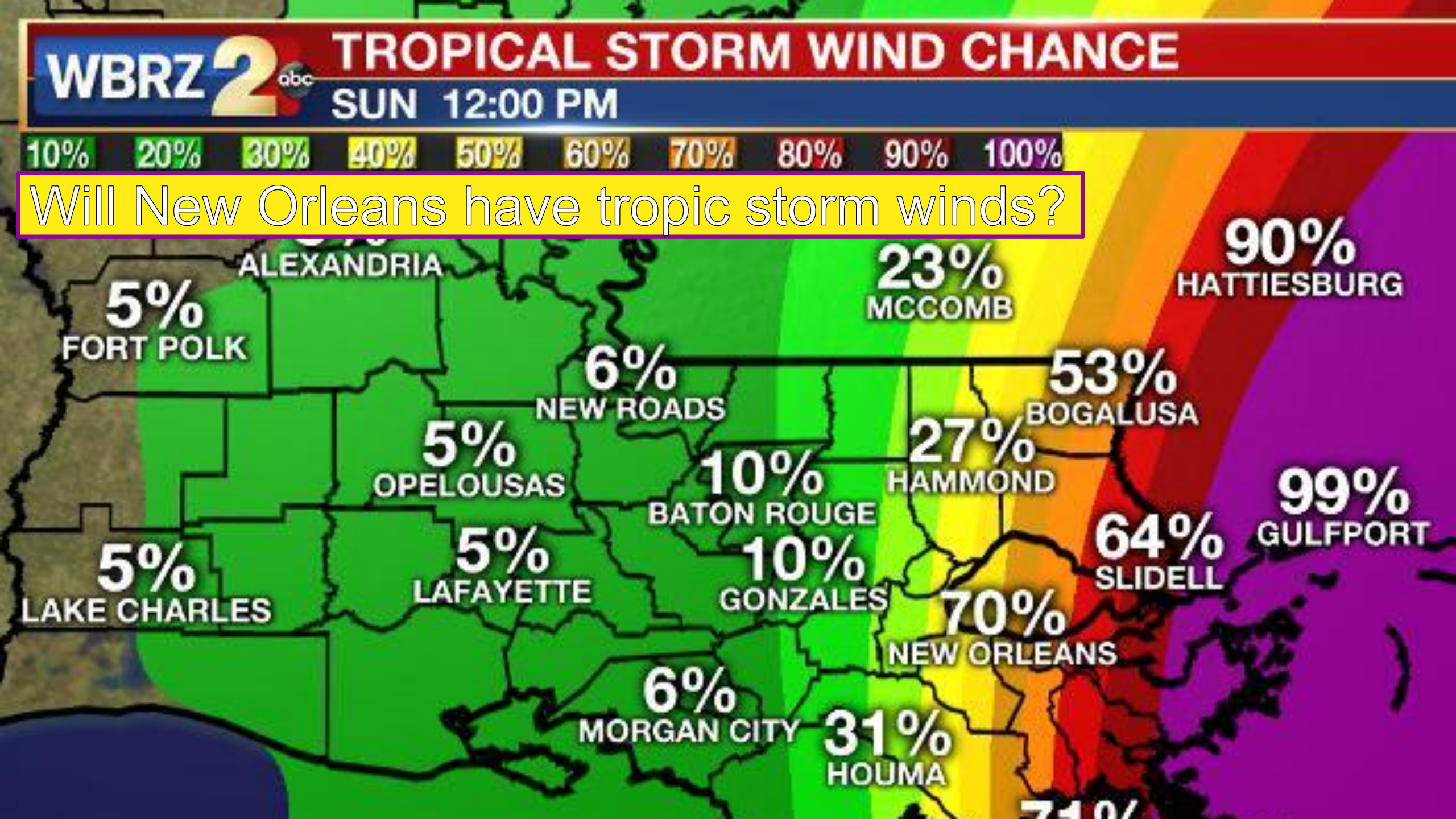
As we saw (Slide 16 ), the precision of AST is inherently limited due to biological phenomena. Even though this is true, we need to draw the line somewhere. But where?

Where does blue become green?

AST breakpoints

The goal of the breakpoint is to predict clinical efficacy of an antibiotic for treating an infection.

AST is inherently imprecise. Additionally, patients are inherently variable in terms of their drug metabolism, immune function, site of infection, and pathogen load.


WBRZ 2 abc
TROPICAL STORM WIND CHANCE
SUN 12:00 PM
10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
Will New Orleans have tropic storm winds?
ALEXANDRIA
5%
FORT POLK
23%
MCCOMB
90%
HATTIESBURG
6%
NEW ROADS
53%
BOGALUSA
5%
OPELOUSAS
27%
HAMMOND
10%
BATON ROUGE
99%
GULFPORT
5%
LAKE CHARLES
5%
LAFAYETTE
10%
GONZALES
64%
SLIDELL
70%
NEW ORLEANS
6%
MORGAN CITY
31%
HOUMA

AST breakpoints

The “breakpoint” is where we choose to draw the line between “susceptible” and “resistant.”

The closer to the results are to the breakpoint, the greater the uncertainty of the interpretation.

Often an “intermediate” category is added, which is a buffer zone that helps with the inherent fuzziness of results and interpretations.

AST interpretive categories

Resistant

Antibiotic A is expected to be ineffective for the treatment of Bacterium B

Susceptible

Antibiotic A is expected to be effective for the treatment of Bacterium B

Intermediate

It is not clear based on *in vitro* testing if Antibiotic A would be effective for the treatment of Bacterium B

AST interpretive categories

Susceptible dose dependent (SDD)

Antibiotic A is expected to be effective for the treatment of Bacterium B if administered to achieve high drug exposure (higher and/or more frequent dosing)

Nonsusceptible

It is not clear based on *in vitro* testing if Antibiotic A would be effective for the treatment of Bacterium B; typically only used when resistance is uncommon.

Not susceptible

When “intermediate” and “resistant” are lumped together into a single interpretive category, they can be lumped into the “not susceptible” category

AST interpretive categories

Intrinsic resistance

Antibiotic A is always considered ineffective for the treatment of Bacterium B. Typically, these antibiotics are not tested or reported for the bacterium. If they are reported, then they can simply be reported as “resistant.”

AST errors

Very major error

Interpreting a resistant antimicrobial as “susceptible”
Outcome: Potentially treating with an inadequate antibiotic

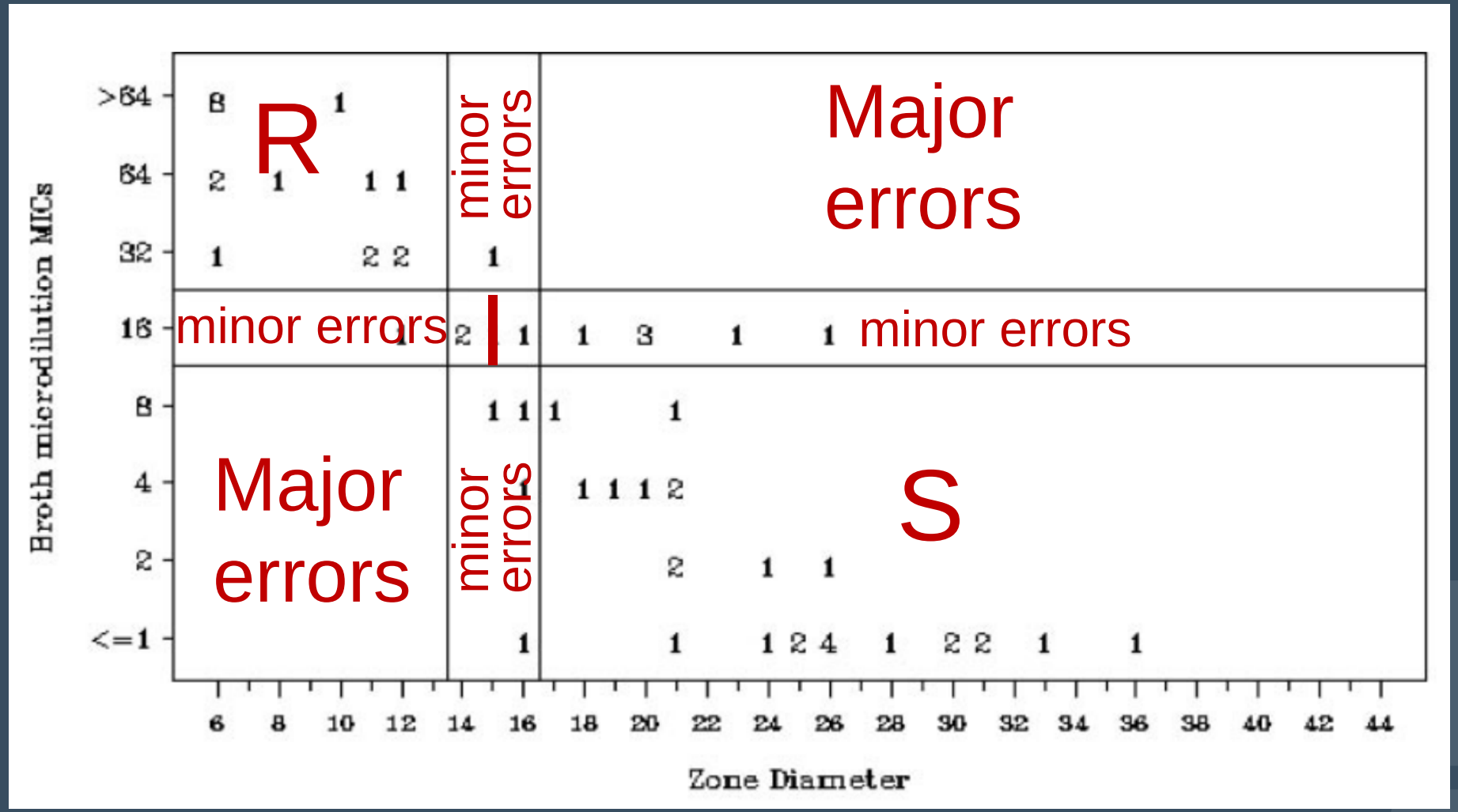
Major error

Interpreting a susceptible antimicrobial as “resistant”
Outcome: Potentially treating with a suboptimal antibiotic

Minor error

Any error involving an “intermediate” interpretation
Outcome: Uncertain

AST errors

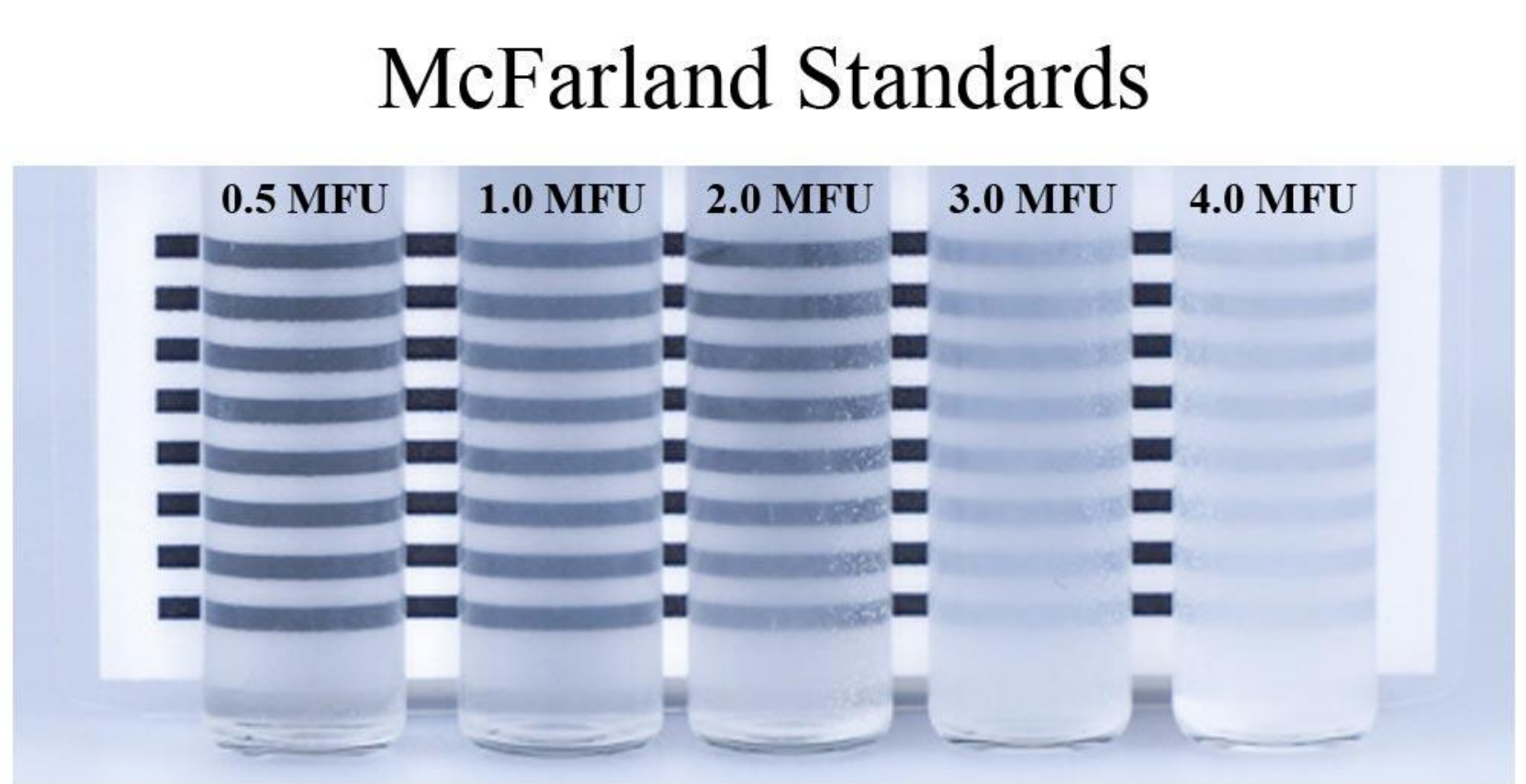


https://jcm.asm.org/content/jcm/45/2/340.full.pdf

Translating visual AST data into results

Translating visual AST data into results

AST methodology



0.5 McFarland (~1.5 x 10^8 cfu/ml) suspension of isolated colonies ("pure culture") is typically used as a starting point for all routine AST.

AST methodology

Disk diffusion

AST methodology
Disk diffusion

Technique

- Use a wrung swab to streak 0.5 McFarland suspension in 3 directions to create a confluent “lawn” of bacteria that will grow on Mueller Hinton agar.
- Drop or place paper antibiotic disks onto the agar surface
  - DO NOT MOVE DISKS AFTER THEY TOUCH THE AGAR
  - Disks may need to be gently tamped down, so they do not fall off
- Invert plate and incubate at 35 °C for 16 to 20 hours
- Measure diameter of the zone of inhibition
  - Measure the back of the inverted plate using a ruler or calipers
  - Use reflected light over a black background
  - Examine without magnification
  - Identify the area that includes complete inhibition
  - Measure using whole millimeters as the unit

Reference document: CLSI M02, 13th edition. Performance standards for antimicrobial disk susceptibility tests, page 23

AST methodology
Disk diffusion

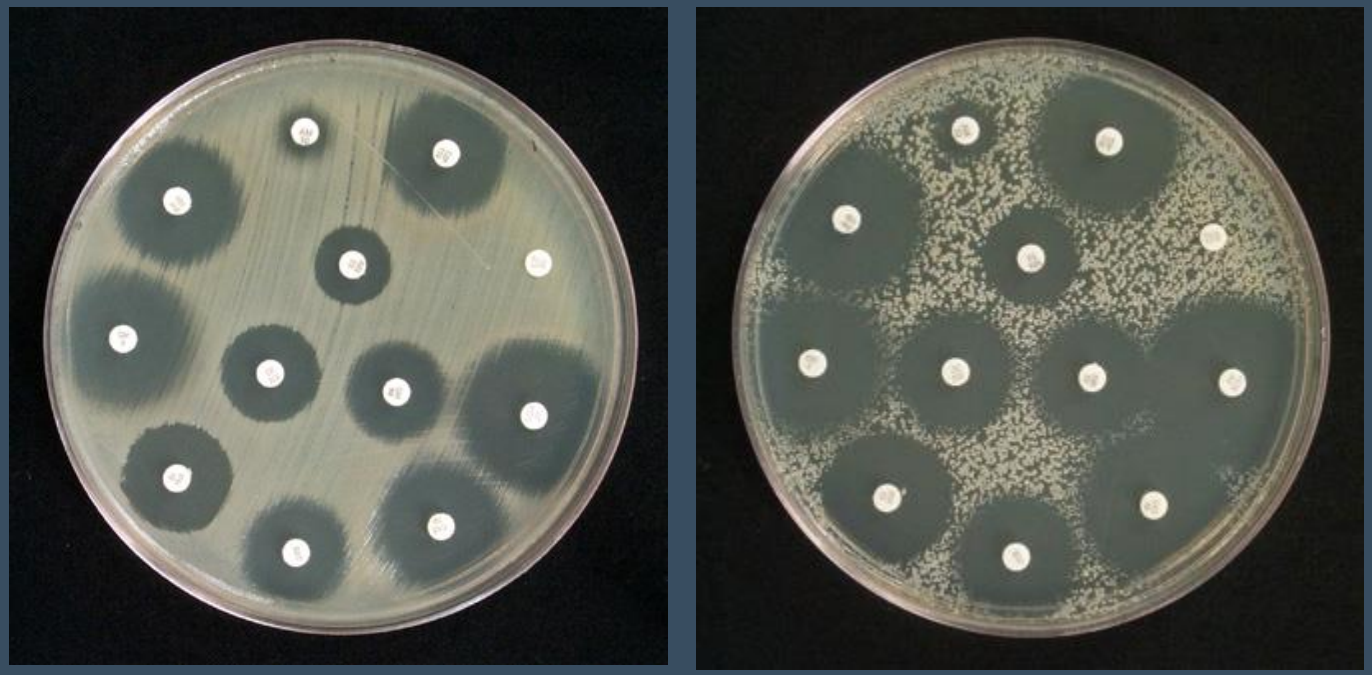
Exceptions

- Invert plate and incubate at 35 °C for 16 to 20 hours
  - Cefoxitin & staphylococci (not *S. aureus*) incubation for 24 hours
  - Vancomycin & enterococci incubation for 24 hours
- Measure diameter of the zone of inhibition
  - Measure the back of the inverted plate using a ruler or calipers
    - Opaque agar (Mueller-Hinton with blood) measured from the front of the plate with the lid removed. Measure growth & ignore hemolysis.
  - Use reflected light over a black background
    - Linezolid & staphylococci read with transmitted light
  - Examine without magnification
  - Identify the area that includes complete inhibition
    - Trimethoprim/sulfamethoxazole (SXT) read at 80% inhibition
    - Ignore the “swarm” of *Proteus* spp. when measuring
  - Measure using whole millimeters as the unit

Reference document: CLSI M02, 13th edition. Performance standards for antimicrobial disk susceptibility tests, page 23

AST methodology

Disk diffusion

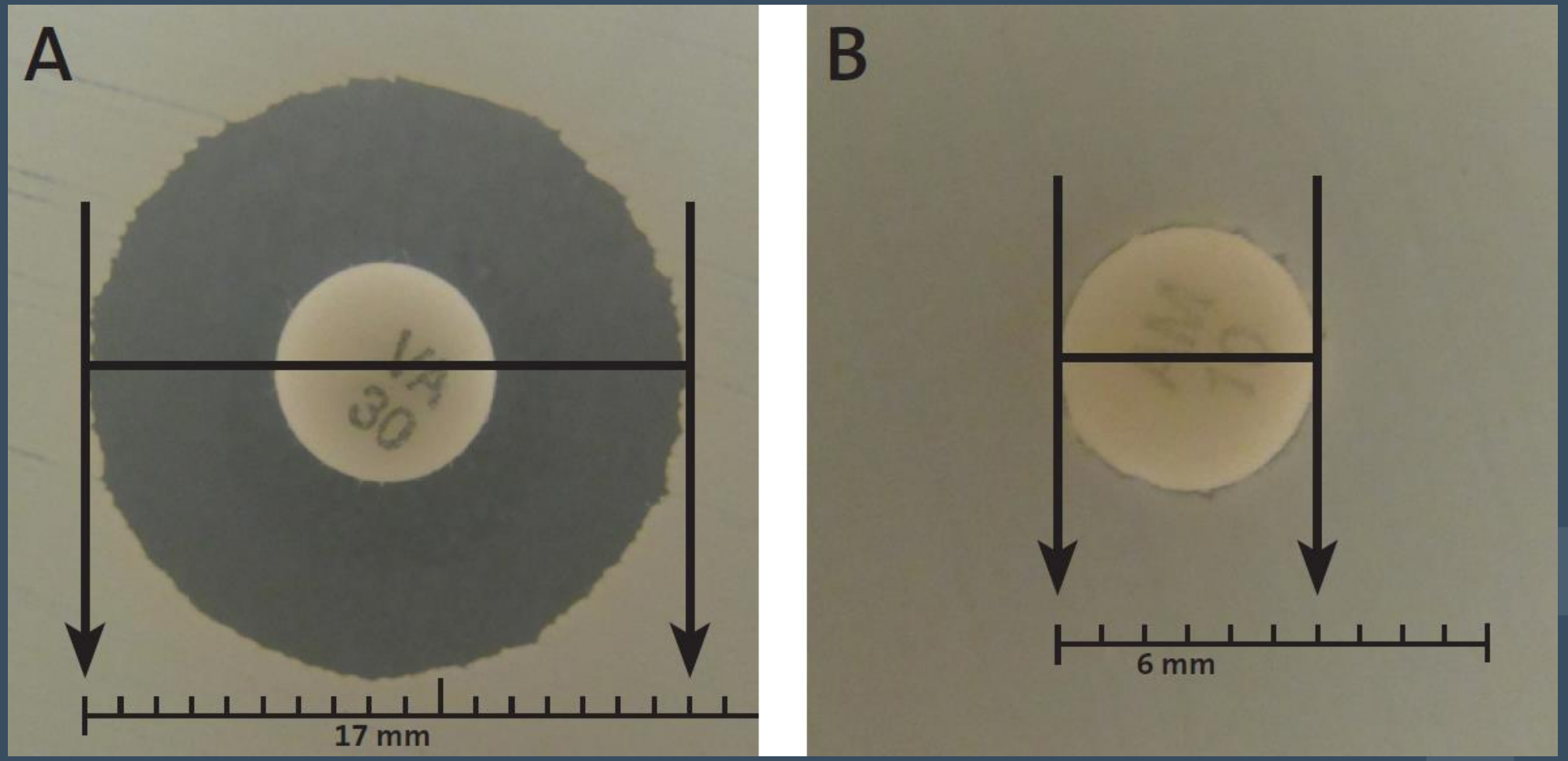


Left = good confluent growth

Right = repeat the test

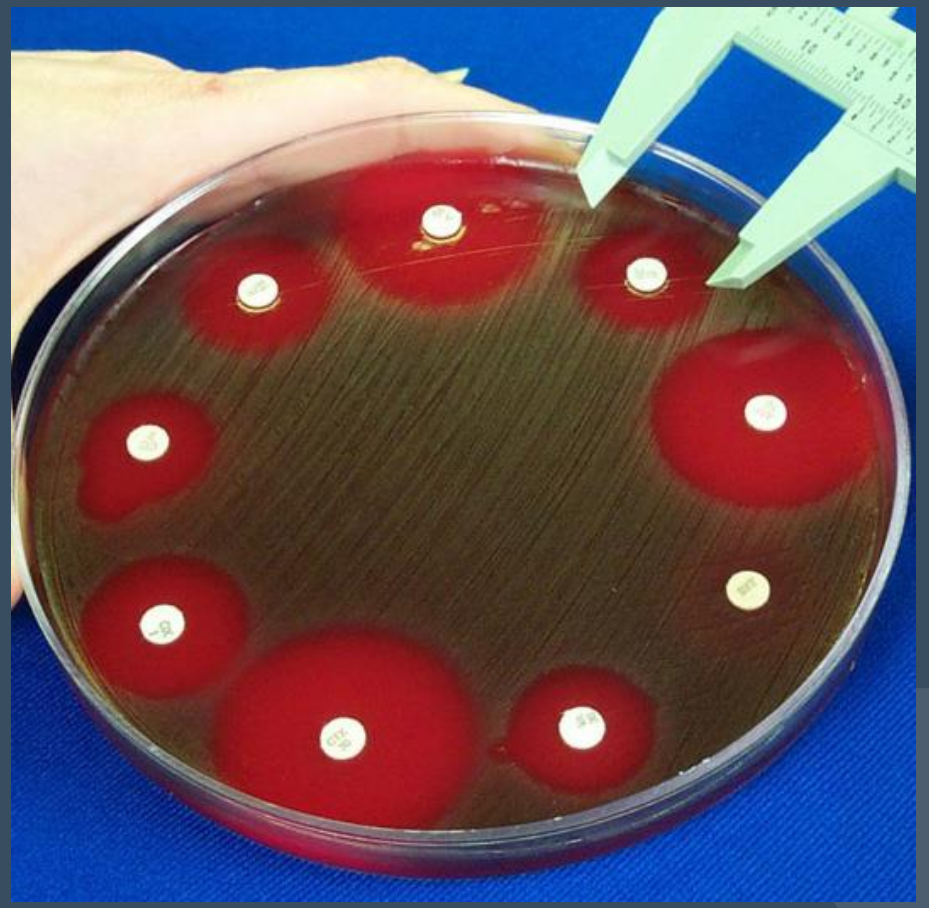
Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

AST methodology
Disk diffusion



Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

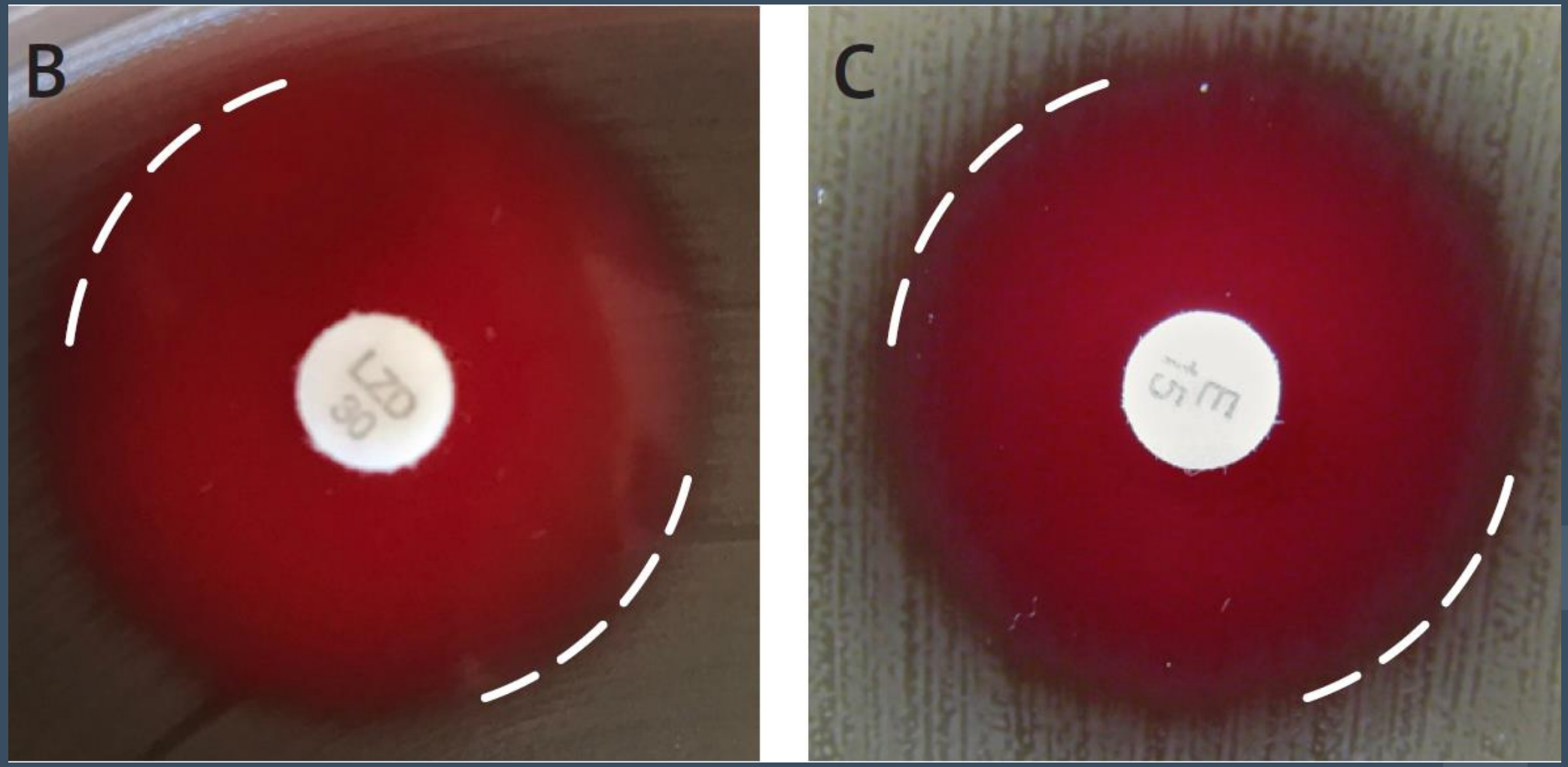
AST methodology
Disk diffusion



Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

AST methodology

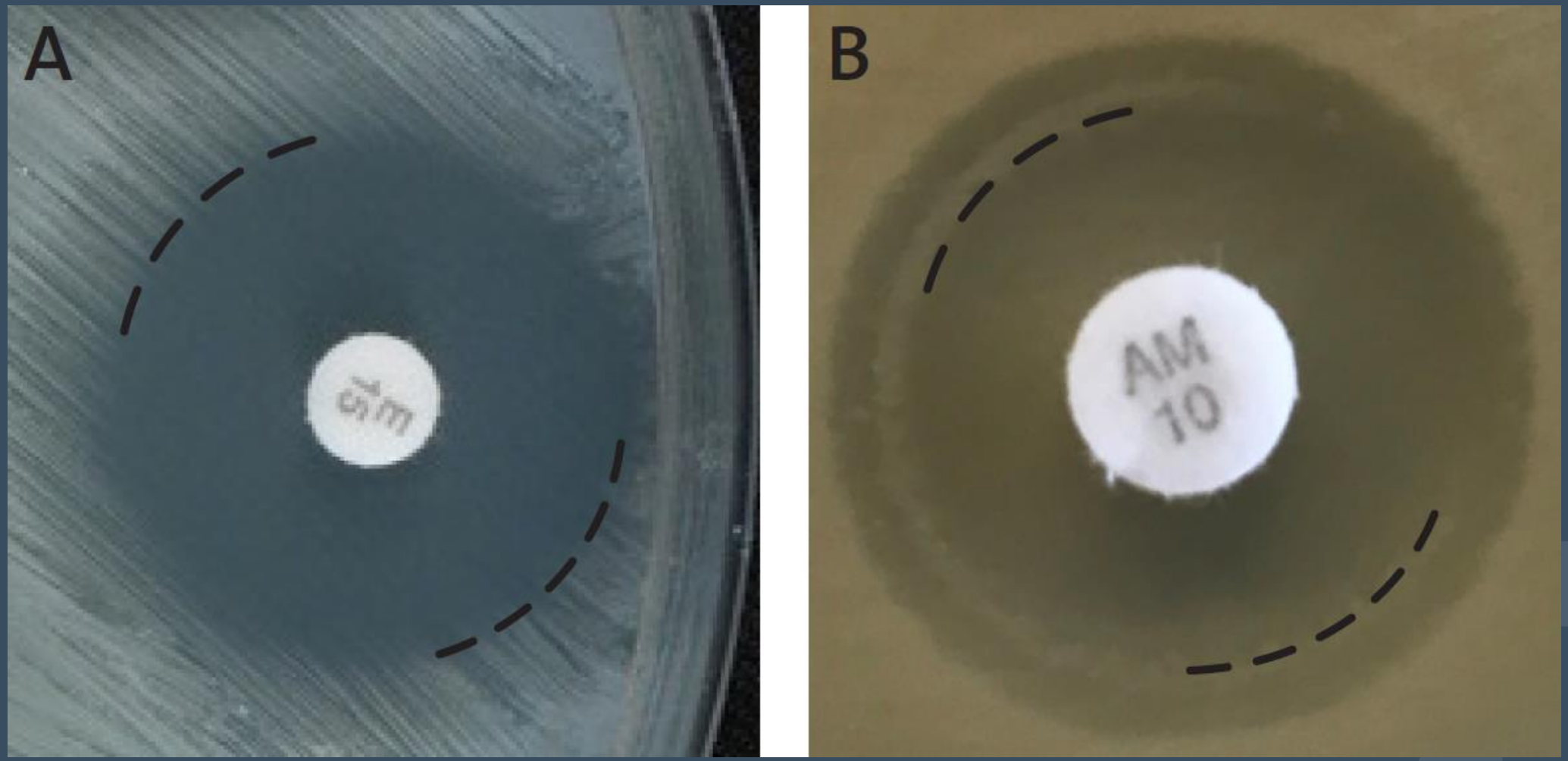
Disk diffusion



Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

AST methodology

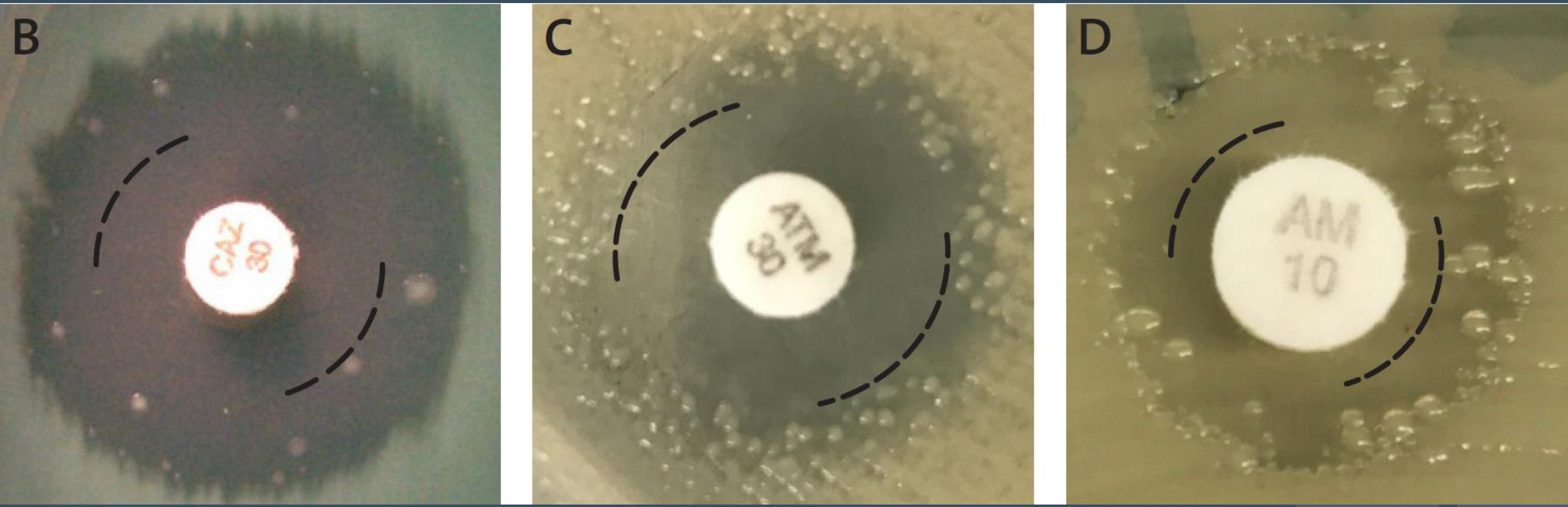
Disk diffusion



Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

AST methodology

Disk diffusion

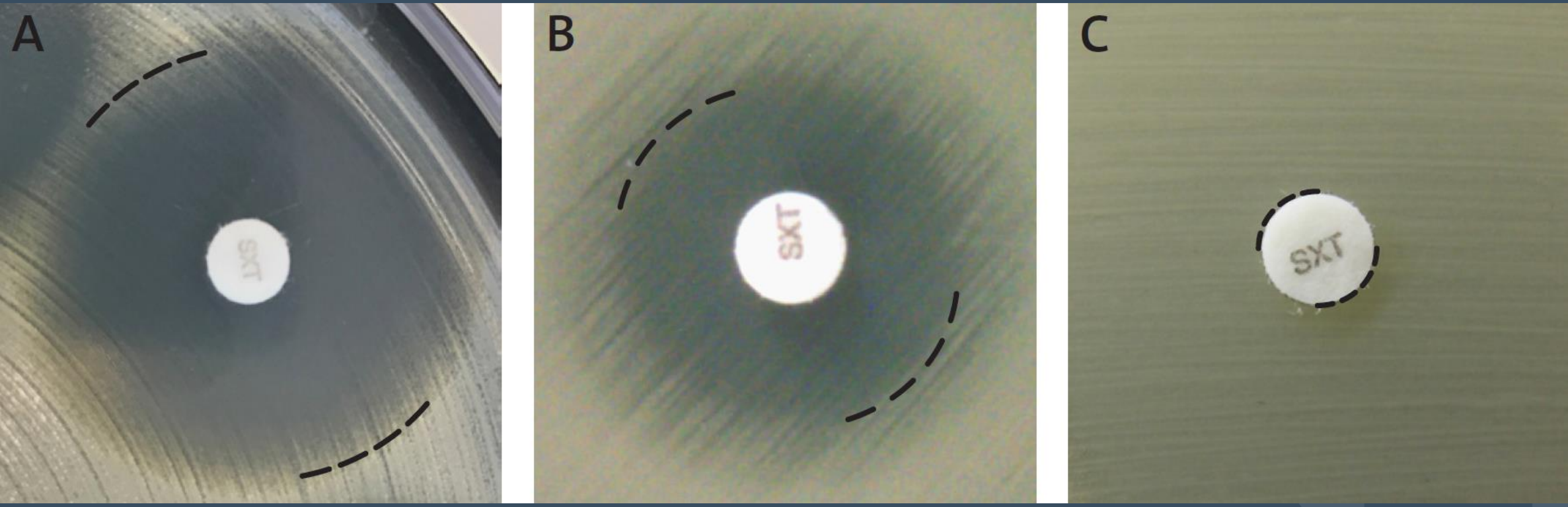


Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

AST methodology

Disk diffusion

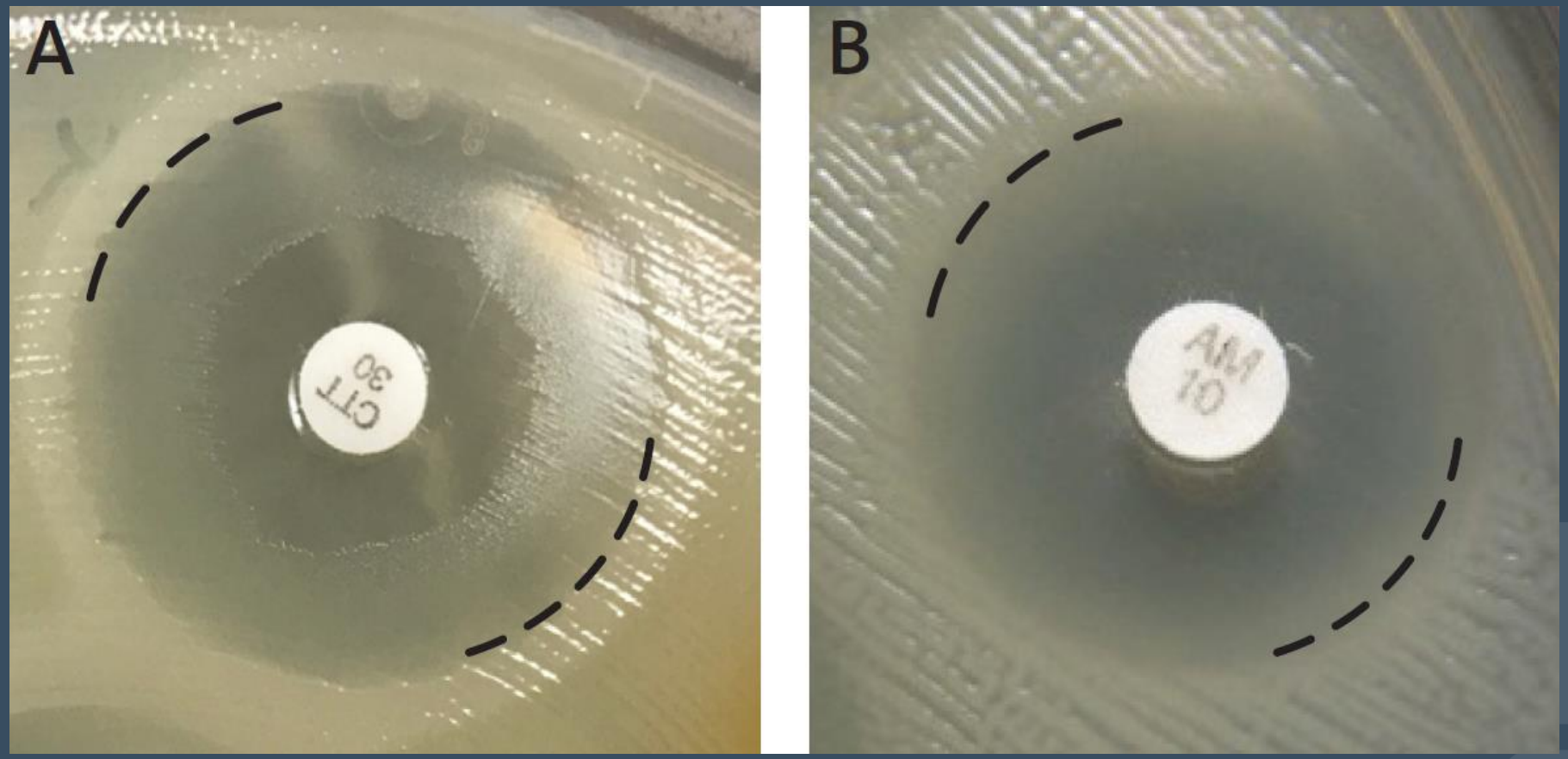
EXCEPTION: Trimethoprim/sulfamethoxazole (SXT) read at 80% inhibition



Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

AST methodology
Disk diffusion

EXCEPTION: Ignore the “swarm” of *Proteus* spp. when measuring



Reference document: CLSI M02QG:2018 QUICK GUIDE — Disk Diffusion Reading Guide, 1st ed.

AST methodology
Broth microdilution (BMD)

Technique

- Antibiotic concentrations start a 1 µl/ml (aka 1 mg/L) and double or halve:
  - 1, 2, 4, 8, 16, 32, 64, 128
  - 1, 0.5, 0.25, 0.12, .06. 0.03
- Final volume is 100 µl per well
- Select 3-5 colonies or grow a broth culture to create a 0.5 McFarland suspension
- Add ~ 5 x 10^5 cfu to each microtiter well.
- Incubate at 35 °C for 16 to 20 hours
- Read the well with no growth as the MIC

Reference document: CLSI M07-A10, 10th edition. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically

AST methodology
Broth microdilution (BMD)

Exceptions

- Incubate at 35 °C for 16 to 20 hours
  - Vancomycin for enterococci incubate for 24 hours
  - Oxacillin for staphylococci incubate for 24 hours
- Read the well with no growth as the MIC
  - Gram positive cocci may have “trailing” growth with chloramphenicol, clindamycin, erythromycin, linezolid, and tetracycline.
  - SXT should be read at 80% inhibition

Reference document: CLSI M07-A10, 10th edition. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically

AST methodology
SXT

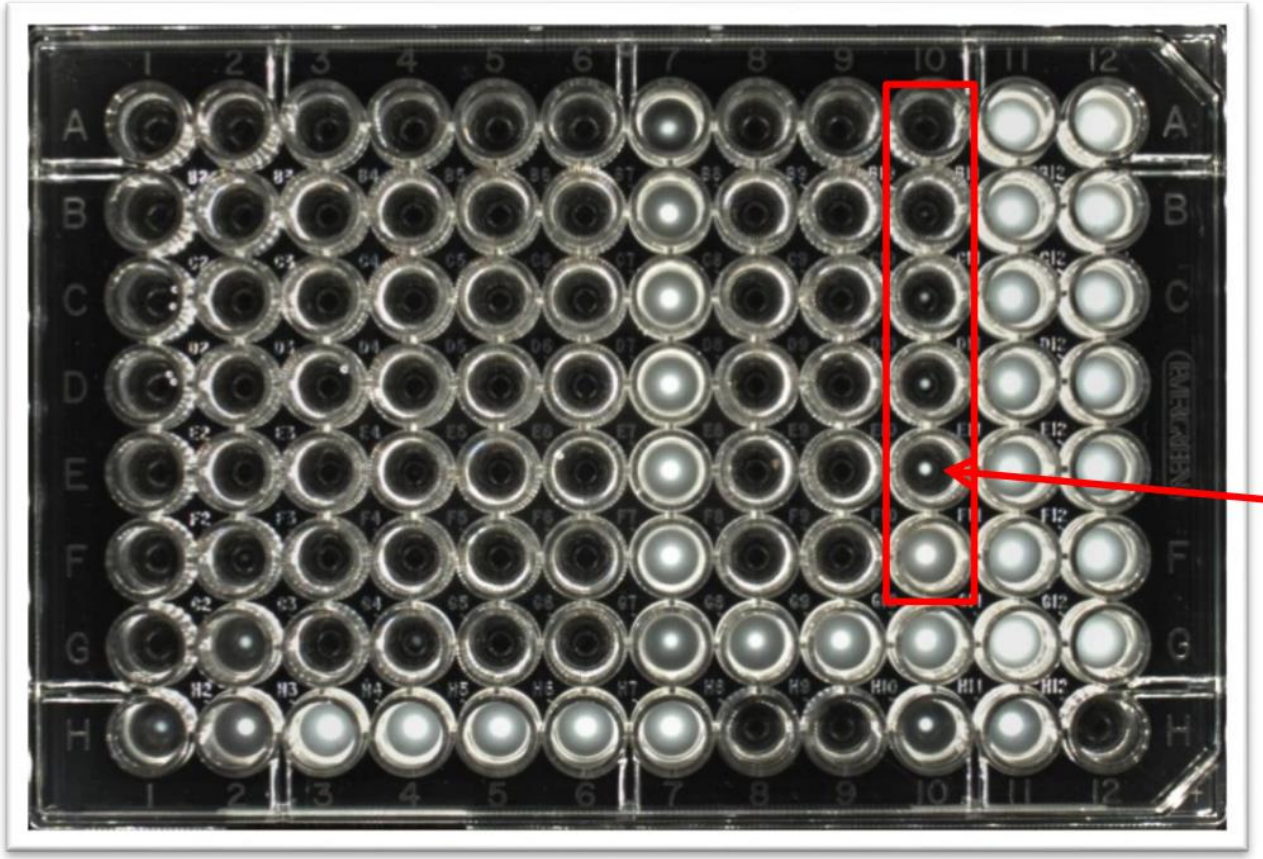


Figure 2. Trimethoprim-Sulfamethoxazole: 80% Inhibition End Point (A10–F10, 152/8–9.5/0.5 µg/mL), MIC = E10

Reference document: CLSI M07-A10, 10th edition. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically

AST methodology

Trailing endpoint

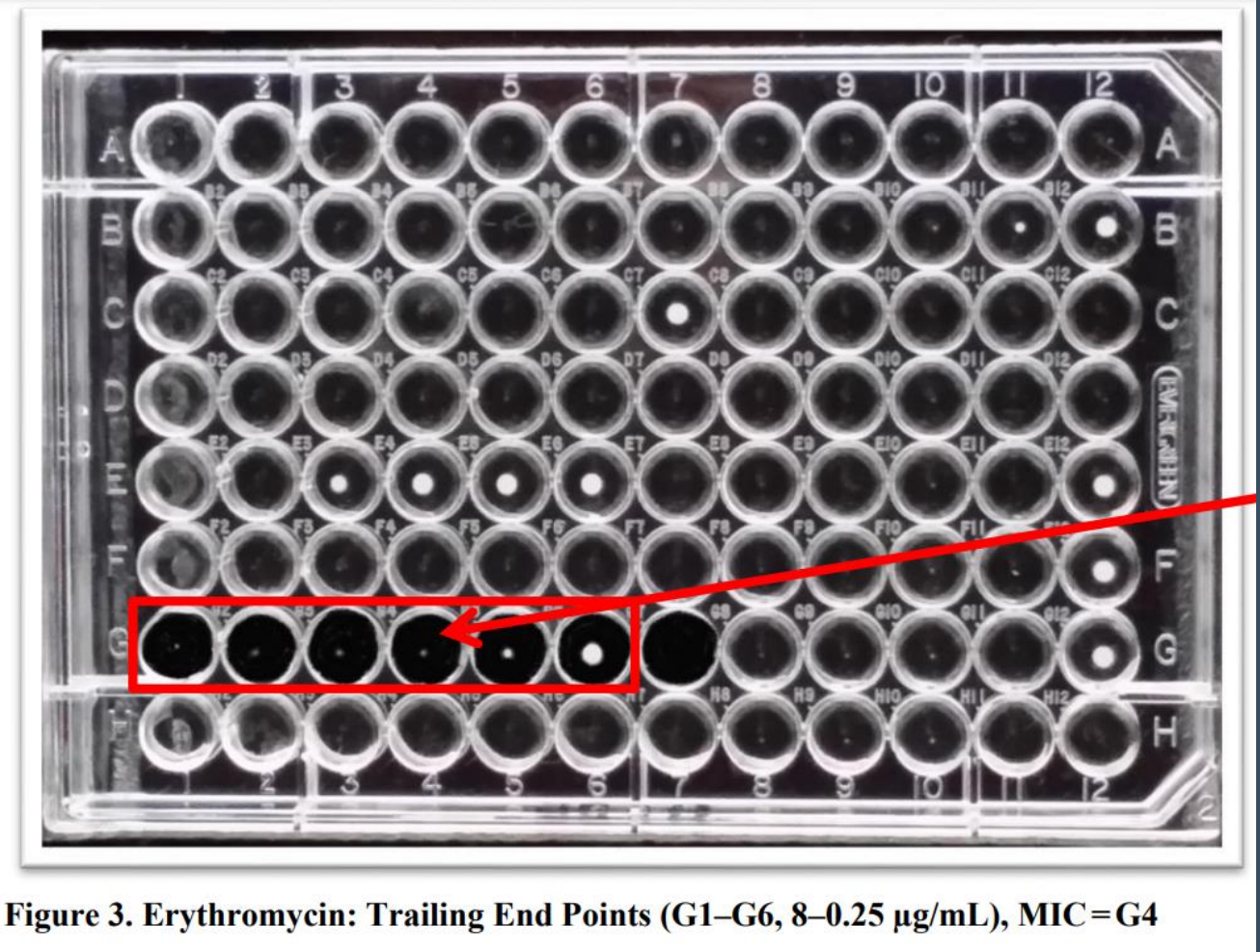


Figure 3. Erythromycin: Trailing End Points (G1–G6, 8–0.25 µg/mL), MIC = G4

Reference document: CLSI M07-A10, 10th edition. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically

AST methodology

Trailing endpoint

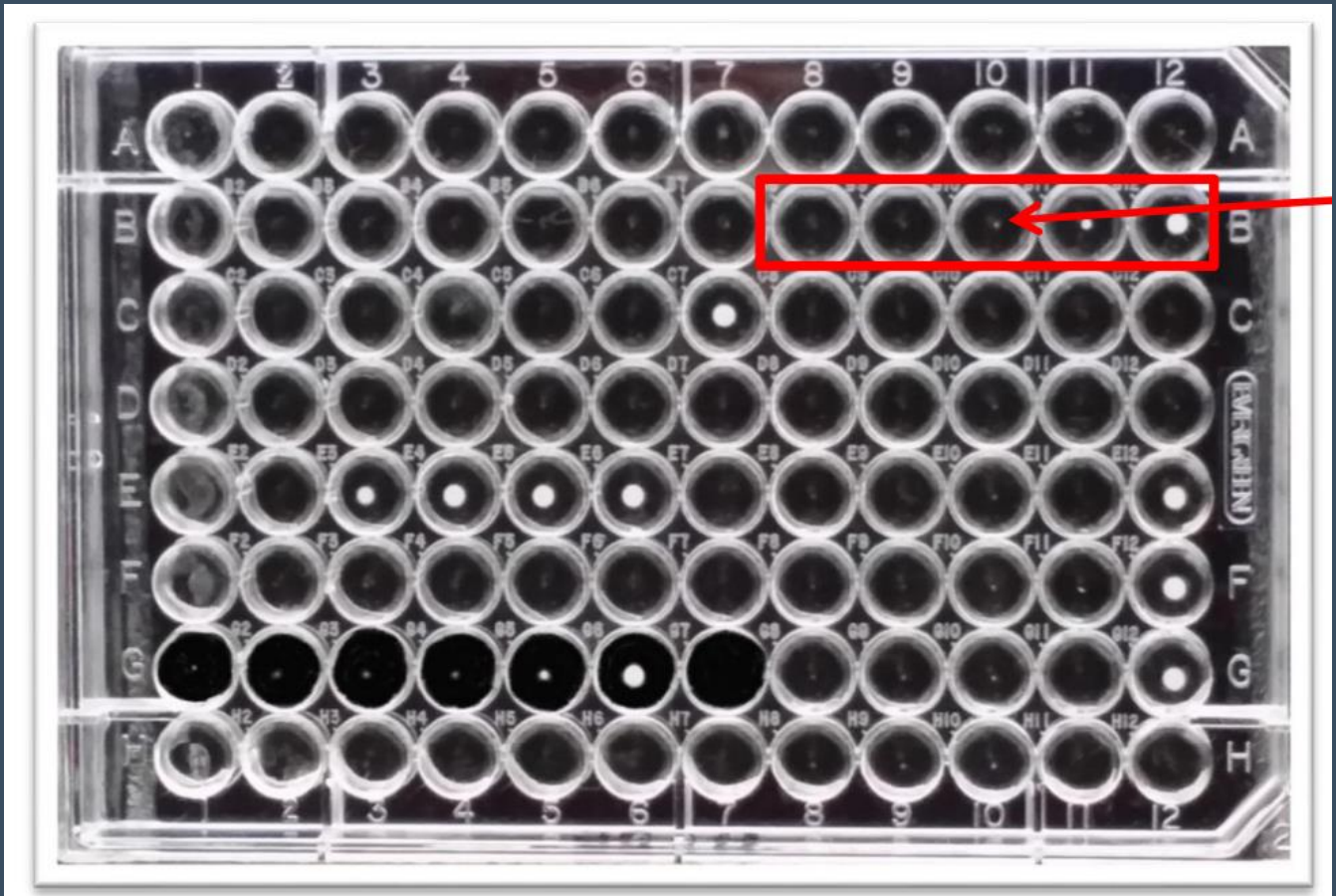


Figure 4. Linezolid: Trailing End Points (B8–B12, 16–1 µg/mL), MIC = B10

Reference document: CLSI M07-A10, 10th edition. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically

AST methodology
It's complicated ¯_(ツ)_/¯

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

(4) Historically, resistance to the penicillinase-stable penicillins (see Glossary I) has been referred to as "methicillin resistance" or "oxacillin resistance." MRSA are strains of *S. aureus* that express *mecA, mecC,* or another mechanism of methicillin **(oxacillin)** resistance, such as changes in affinity of penicillin-binding proteins for oxacillin (modified *S. aureus* strains).

(5) Most **methicillin** (oxacillin) resistance is mediated by *mecA,* encoding PBP2a (also called PBP2'). Isolates that test positive for *mecA* or PBP2a should be reported as **methicillin** (oxacillin) resistant (see Appendix H).

Detection of **methicillin** (oxacillin) resistance in staphylococci is achieved by using specific methods as listed in Table 2C and further described in Table 3**F**.

Organism	Methods for Detection of Methicillin (Oxacillin)-Resistant *Staphylococcus* spp.				
	Cefoxitin MIC	Cefoxitin disk diffusion	Oxacillin MIC	Oxacillin disk diffusion	Oxacillin salt agar
S. aureus	Yes **(16–20 h)**	Yes **(16–18 h)**	Yes **(24 h)**	No	Yes **(24 h)**
S. lugdunensis	Yes **(16–20 h)**	Yes **(16–18 h)**	Yes **(24 h)**	No	No
S. epidermidis	No	Yes **(24 h)**	Yes **(24 h)**	Yes **(16–18 h)**	No
S. pseudintermedius	No	No	Yes **(24 h)**	Yes **(16–18 h)**	No
S. schleiferi	No	No	Yes **(24 h)**	Yes **(16–18 h)**	No
Other *Staphylococcus* spp. (not listed above)	No	Yes[a] **(24 h)**	Yes[a] **(24 h)**	No	No

Abbreviations: h, hour(s); MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant staphylococci; PBP2a, penicillin-binding protein 2a.

[a] For isolates of "other *Staphylococcus* spp." from serious infections for which the oxacillin MICs are 0.5–2 µg/mL, testing for *mecA* or PBP2a should be considered (see comment [17]). Cefoxitin disk diffusion is not currently recommended.

Mechanisms of **methicillin** (oxacillin) resistance other than *mecA* are rare and include a novel *mecA* homologue, *mecC*.[4] MICs for strains with *mecC* are typically cefoxitin resistant and oxacillin susceptible; *mecC* resistance cannot be detected by tests directed at *mecA* or PBP2a.

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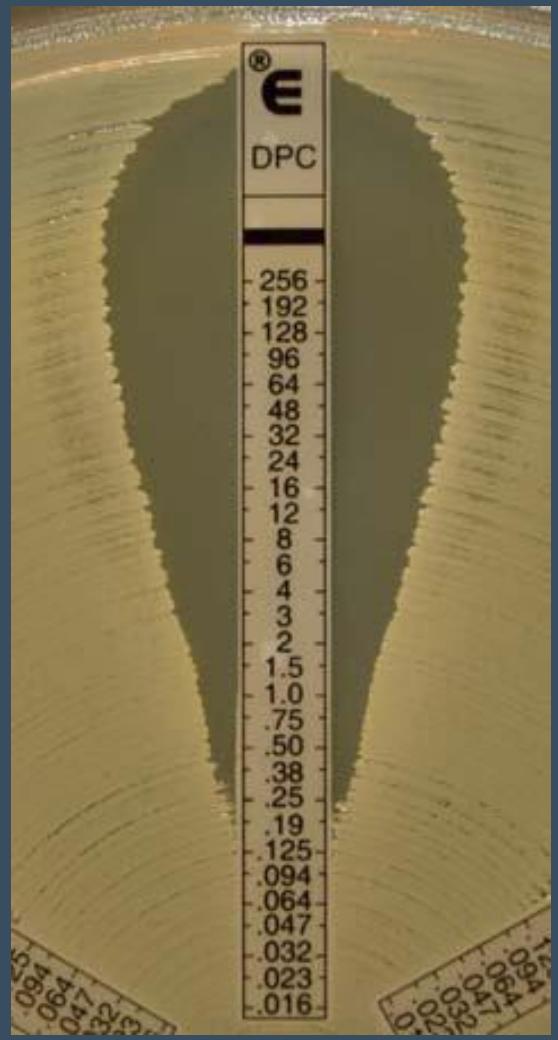
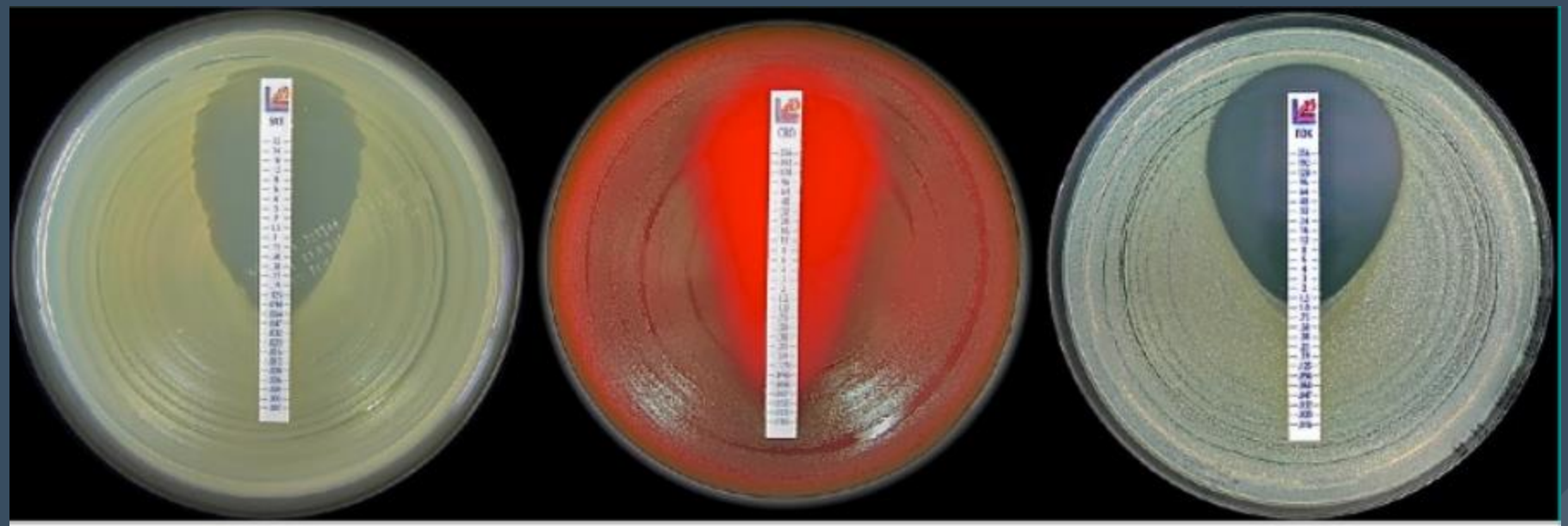
Commercial AST methods

Epsilometer test (Etest®)



Commercial AST methods

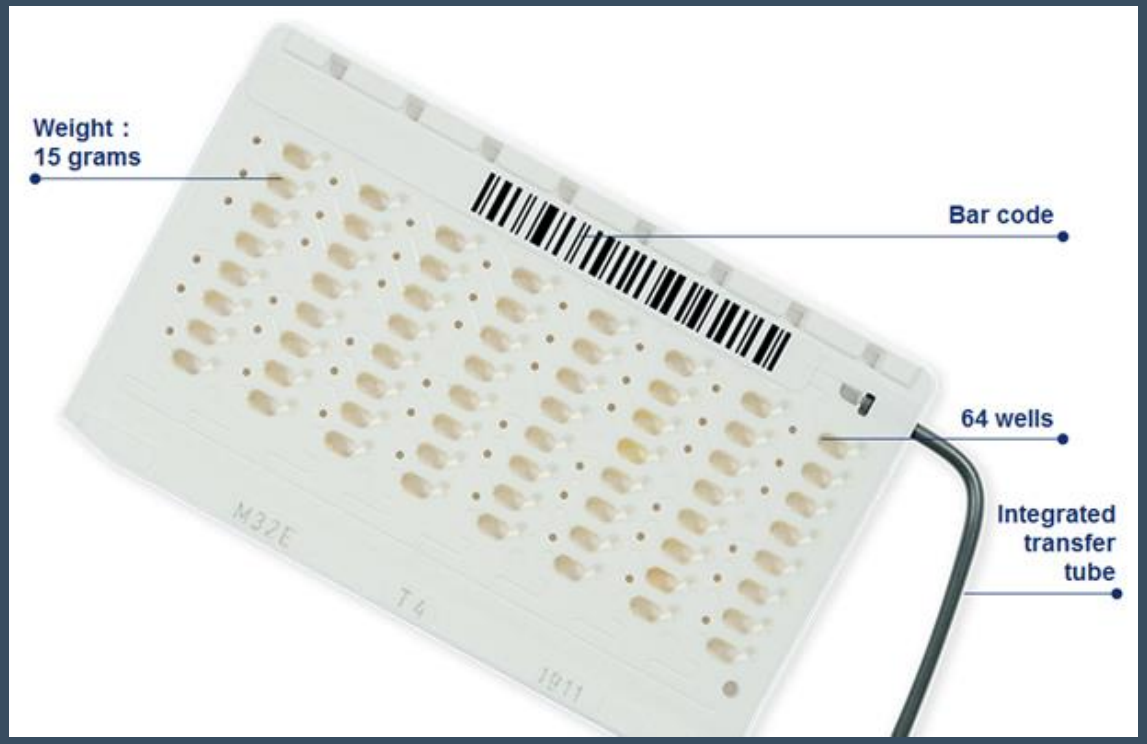
Liofilchem MIC Test Strip (MTS™)



E. coli ATCC® 25922	*S. pneumoniae* ATCC® 49619	*S. aureus* ATCC® 29213
MTS™ SXT 0.002-32 µg/mL	MTS™ CRO 0.016-256 µg/mL	MTS™ FOX 0.016 - 256 µg/mL
M.I.C. = 0.094 µg/mL	M.I.C. = 0.064 µg/mL	M.I.C. = 1.5 µg/mL

Commercial AST methods

Vitek® 2



Commercial AST methods

Phoenix®

Commercial AST methods

MicroScan® WalkAway

Commercial AST methods

Sensititre™ Vizion™ (aka Trek)

AST standard setting organizations

FDA

U.S. Food & Drug Administration

CLSI

Clinical & Laboratory Standards Institute

EUCAST

European Committee on Antimicrobial Susceptibility Testing

FDA breakpoints

Susceptibility interpretation

	Minimum Inhibitory Concentrations (mcg/mL)			Disk Diffusion (zone diameter in mm)		
Pathogen	S	I	R	S	I	R
Enterobacteriaceae	≤2	4-8[a]	≥16	≥25	19-24[a]	≤18
Pseudomonas aeruginosa [b]	≤8	-	≥16	≥18	-	≤17
Streptococcus pneumoniae (non-meningitis)	M100 standard is recognized			-	-	-
Streptococcus spp β- Hemolytic Group	M100 standard is recognized					
Streptococcus spp Viridans Group	M100 standard is recognized					

https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria

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Susceptibility interpretation

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	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)											
B	Cefepime	30 µg	≥25	19–24	–	≤18	≤2	4–8	–	≥16	**(17)** 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.
B B	Cefotaxime or ceftriaxone	30 µg 30 µg	≥26 ≥23	–	23–25^ 20–22^	≤22 ≤19	≤1 ≤1	–	2^ 2^	≥4 ≥4	**(18)** 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 (12).
B	Cefotetan	30 µg	≥16	–	13–15^	≤12	≤16	–	32^	≥64	
B	Cefoxitin	30 µg	≥18	–	15–17^	≤14	≤8	–	16^	≥32	**(19)** Breakpoints are based on a dosage regimen of at least 8 g per day (eg, 2 g administered every 6 h).
B	Cefuroxime (parenteral)	30 µg	≥18	–	15–17^	≤14	≤8	–	16^	≥32	**(20)** Breakpoints are based on a dosage regimen of 1.5 g administered every 8 h. See comment (12).
C	Ceftazidime	30 µg	≥21	–	18–20^	≤17	≤4	–	8^	≥16	**(21)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h. See comment (12).
O	Cefamandole	30 µg	≥18	–	15–17^	≤14	≤8	–	16^	≥32	See comment (12).
O	Cefmetazole	30 µg	≥16	–	13–15^	≤12	≤16	–	32^	≥64	**(22)** Insufficient new data exist to reevaluate breakpoints listed here.
O	Cefonicid	30 µg	≥18	–	15–17^	≤14	≤8	–	16^	≥32	See comment (12).
O	Cefoperazone	75 µg	≥21	–	16–20	≤15	≤16	–	32	≥64	See comment (12).
O	Ceftizoxime	30 µg	≥25	–	22–24^	≤21	≤1	–	2^	≥4	**(23)** Breakpoints are based on a dosage regimen of 1 g administered every 12 h. See comment (12).
O	Moxalactam	30 µg	≥23	–	15–22^	≤14	≤8	–	16–32^	≥64	See comment (12).

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Intrinsic resistance tables (very helpful)

B1. Enterobacterales

Organism \ Antimicrobial Agent	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Ticarcillin	Cephalosporins I: Cefazolin, Cephalothin	Cephamycins: Cefoxitin, Cefotetan	Cephalosporin II: Cefuroxime	Imipenem	Tetracyclines	Tigecycline	Nitrofurantoin	Polymyxin B Colistin	Aminoglycosides
Citrobacter freundii	R	R	R		R	R	R						
Citrobacter koseri, *Citrobacter amalonaticus* group[a]	R			R									
Enterobacter cloacae complex[b]	R	R	R		R	R							
Escherichia coli	There is no intrinsic resistance to β-lactams in this organism.												
Escherichia hermannii	R			R									
Hafnia alvei	R	R	R		R	R							
Klebsiella (formerly *Enterobacter*) *aerogenes*	R	R	R		R	R							
Klebsiella pneumoniae, *Klebsiella oxytoca*, *Klebsiella variicola*	R			R									
Morganella morganii	R	R			R		R	[c]		R	R	R	
Proteus mirabilis	There is no intrinsic resistance to penicillins and cephalosporins in this organism.							[c]	R	R	R	R	
Proteus penneri	R				R		R	[c]	R	R	R	R	
Proteus vulgaris	R				R		R	[c]	R	R	R	R	
Providencia rettgeri	R	R			R			[c]	R	R	R	R	
Providencia stuartii	R	R			R			[c]	R	R	R	R	[d]
Raoultella spp.[e]	R			R									

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Intrinsic resistance tables (very helpful)

B1. Enterobacterales (Continued)

Organism \ Antimicrobial Agent	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Ticarcillin	Cephalosporins I: Cefazolin, Cephalothin	Cephamycins: Cefoxitin, Cefotetan	Cephalosporin II: Cefuroxime	Imipenem	Tetracyclines	Tigecycline	Nitrofurantoin	Polymyxin B Colistin	Aminoglycosides
Salmonella and *Shigella* spp.	There is no intrinsic resistance to β-lactams in these organisms; refer to **WARNING** below for reporting.												
Serratia marcescens	R	R	R		R	R	R				R	R	
Yersinia enterocolitica	R	R		R	R								

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Intrinsic resistance tables (very helpful)

B2. Non-Enterobacterales

Organism \ Antimicrobial Agent	Ampicillin, Amoxicillin	Piperacillin	Ticarcillin	Ampicillin-sulbactam	Amoxicillin- clavulanate	Piperacillin-tazobactam	Cefotaxime	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Imipenem	Meropenem	Ertapenem	Polymyxin B Colistin	Aminoglycosides	Tetracyclines/ Tigecycline	Trimethoprim	Trimethoprim-sulfamethoxazole	Chloramphenicol	Fosfomycin
Acinetobacter baumannii/ Acinetobacter calcoaceticus complex	R				R						R			R				R		R	R
Burkholderia cepacia complex[a]	R	R	R	R	R	[a]	[a]	[a]		[a]	[a]	[a]		R	R	[a]		[a]			R
Pseudomonas aeruginosa	R			R	R		R	R						R			R	R	R	R	
Stenotrophomonas maltophilia	R	R	R	R	R	R	R	R			R	R	R	R		R	[b]	R			R

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Details

Sometimes, multiple antibiotics are combined for “synergy.” Rarely is there evidence to support this practice, and typically it is generally frowned upon. The exception where it is accepted and practiced routinely is enterococcal endocarditis (gentamicin synergy).

Details

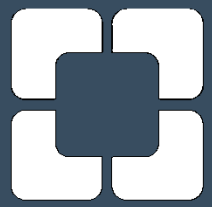
Some antibiotics kill bacteria; these are bactericidal. Some antibiotics keep bacteria from growing without killing them; these are bacteriostatic. –cidal drugs are theoretically "better" than –static drugs, but this is more of a feeling than an evidenced-based opinion.

https://doi.org/10.1093/cid/cix1127

Details

Sometimes one drug's susceptibility can predict susceptibility to another drug.

A common example is that tetracycline susceptibility can predict susceptibility to doxycycline. However, tetracycline resistance with doxycycline susceptibility is possible.



Cleveland Clinic

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