TURNING THE TIDE: ADVANCING LAB DIAGNOSTICS THROUGH BREAKPOINTS & STEWARDSHIP

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US Medical Affairs
Medical Advisor

DISCLOSURE

- I am an employee of bioMérieux

LEARNING OBJECTIVES

Understand the clinical and societal implications of breakpoint management in the context of antimicrobial resistance

Describe the current susceptibility breakpoint landscape in terms of regulatory requirements and current clinical application

Discuss the definition, rationale, and methodologies for diagnostic stewardship

OUR COMPANY PURPOSE

WE HELP MAKE THE WORLD A HEALTHIER PLACE

Our dedication to public health is the thread that connects everything we do

- ☑ Serve the greater good for mankind
- ☑ Place medicine at the interest of patients first and foremost
- ☑ Meet global public health needs, particularly in the field of infectious diseases

ANTIMICROBIAL RESISTANCE & BREAKPOINTS

Antimicrobial resistance (AMR) is a global issue that threatens patient safety and public health

Key element to confront and manage AMR: detect & interpret resistance

Breakpoints are a moving target

BREAKPOINTS: LANDSCAPE IN THE US

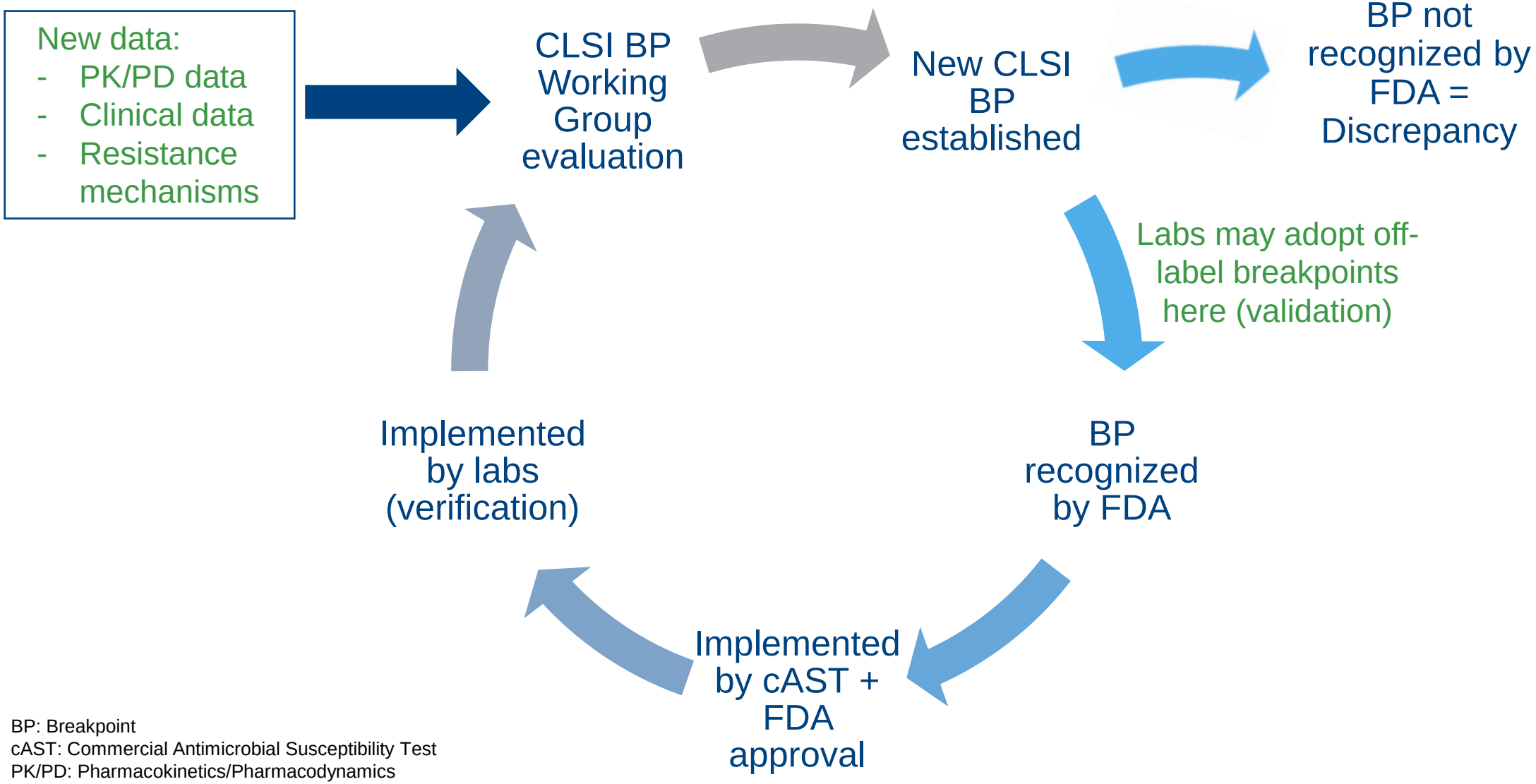
US REGULATIONS

- Determines breakpoints of new antimicrobials
- Authorizes updates of breakpoints (CLSI & cAST)

- Reviews new data/publications
- Creates laboratory breakpoint standards (M100)
- Collaborates with FDA for breakpoint updates

- Creates best practice checklists for labs
- Inspects clinical labs for compliance

BREAKPOINT UPDATE LIFE CYCLE



BP: Breakpoint
cAST: Commercial Antimicrobial Susceptibility Test
PK/PD: Pharmacokinetics/Pharmacodynamics

Modified from CLSI Presentation: *CLSI 2023 AST Webinar: What's New in M100-Ed33, April 2023*

HOW DO CLSI BPS GET ADOPTED BY FDA?

- CLSI submits CLSI rationale document explaining BPs data to FDA for consideration
- FDA reviews rationale:
  - Agreement → FDA publishes BPs on **S**usceptibility **T**est **I**nterpretive **C**riteria (STIC) website
  - No agreement → FDA publishes exception to CLSI BPs on STIC website
  - Partial agreement → FDA publishes exception to CLSI BPs on STIC website
- FDA review typically takes ~6-24 months after CLSI rationale submitted to FDA

FDA STIC:

FDA STIC WEBSITE EXAMPLE

Cefepime – Injection products

	Minimum Inhibitory Concentrations (mcg/mL)				Disk Diffusion (zone diameter in mm)			
Pathogen	S	SDD	I	R	S	SDD	I	R
Enterobacterales[a]	M100 standard is recognized				M100 standard is recognized			
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							

Content current as of:
08/22/2023

Regulated Product(s)
Drugs

S = Susceptible; SDD= susceptible-dose dependent; I = Intermediate; R = Resistant

WHAT DOES THIS MEAN FOR OUR CUSTOMERS?

Updated BP Status	Commercial AST System Status	Performance Assessment Required[1]
CLSI = FDA	CLSI BPs are FDA cleared and available on panel/software	Verification[2] 10-15 isolates/drug
CLSI = FDA	Device manufacturer has notified customers that device has received FDA clearance with updated CLSI/FDA BPs and has advised customers how to implement BPs with their panels/software	Verification[2] 10-15 isolates/drug
CLSI = FDA	Device manufacturer has **not** received FDA clearance of the device with updated CLSI/FDA BPs	Validation (if desire to use CLSI BPs) 30 isolates/drug
CLSI ≠ FDA	Manufacturer must provide FDA BPs; use of CLSI BPs would be off-label	Validation (if desire to use CLSI BPs) 30 isolates/drug

[1]Consensus suggestions from authors of 2023 Breakpoint Implementation Toolkit (2023 BIT, future release)
[2]If no change to the test has been made by the AST manufacturer (eg, no reformulation of drug dilutions), a verification of reporting may be sufficient. This would involve ensuring MIC results are interpreted correctly on patient reports.

Modified from CLSI Presentation: *CLSI 2023 AST Webinar: What's New in M100-Ed33, April 2023*

CRE: DELAY BETWEEN REVISION & IMPLEMENTATION

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology

CrossMark

Impact of Delays between Clinical and Laboratory Standards Institute and Food and Drug Administration Revisions of Interpretive Criteria for Carbapenem-Resistant *Enterobacteriaceae*

Sarah M. Bartsch,[a] Susan S. Huang,[b] Kim F. Wong,[c] Rachel B. Slayton,[d] James A. McKinnell,[e,f] Daniel F. Sahm,[g] Krystyna Kazmierczak,[g] Leslie E. Mueller,[a] John A. Jernigan,[d] Bruce Y. Lee[a]

Public Health Computational and Operations Research (PHICOR), Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA[a]; Division of Infectious Diseases and Health Policy Research Institute, University of California—Irvine School of Medicine, Orange, Cal
of Pittsburgh, Pittsburgh, Pennsylvania, USA[c]; Division of Healthcare Quality Promotion, Centers for Disease C
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Memorial Medical Center, Torrance, California, USA[f]; International Health Management Associates, Inc., Schau

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Carbapenem-Resistant *Enterobacteriaceae* Detection Practices in California: What Are We Missing?

Romney M. Humphries,[1] Janet A. Hindler,[1] Erin Epson,[2] Sam Horwich-Scholefield,[2] Loren G. Miller,[3,4] Job Mendez,[3] Jeremias B. Martinez,[3] Jacob Sinkowitz,[3] Darren Sinkowtiz,[4] Christina Hershey,[4] Patricia Marquez,[5] Sandeep Bhaurla,[5] Marcelo Moran,[5] Lindsey Pandes,[5] Dawn Terashita,[5] and James A. McKinnell[3,4,5]

[1]Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at the University of California–Los Angeles, [2]Healthcare-Associated Infections Program, California Department of Public Health, [3]LA BioMed at Harbor–University of California–Los Angeles Medical Center, [4]David Geffen School of Medicine at the University of California–Los Angeles, and [5]Acute Communicable Disease Control Program, Healthcare Outreach Unit, Los Angeles County Department of Public Health, California

Bartsch SM, et al. J Clin Microbiol. 2016 Nov;54(11):2757-2762.
Humphries RM, et al. Clin Infect Dis. 2018 Mar 19;66(7):1061-1067.

INTERPRETIVE BREAKPOINT IMPACT

- Humphries, et al. compared categorical interpretation of *Enterobacteriaceae* with elevated minimum inhibitory concentrations by pre- and post-2010 CLSI breakpoints

Table 4. Impact of Use of Historical vs Current Clinical and Laboratory Standards Institute/US Food and Drug Administration Carbapenem Breakpoints for *Enterobacteriaceae*, for a Collection of 421 *Enterobacteriaceae* With Elevated Carbapenem Minimum Inhibitory Concentrations

Carbapenemase	Total	No. "S" to EPM, by Breakpoint		No. "S" to IPM, by Breakpoint		No. "S" to MER, by Breakpoint		No. "S" to All 3 Carbapenems, by Historical Breakpoint	No. "S" to IMP and MER, by Historical Breakpoint
		Historical[a]	Current[b]	Historical	Current	Historical	Current		
IMP	2	0	0	1	0	1	0	0	1
KPC	208	21	1	25	0	42	7	16	22
KPC and OXA	1	0	0	1	0	0	0	0	0
NDM	3	0	0	0	0	0	0	0	0
OXA-48	1	0	0	1	0	0	0	0	0
OXA-232	17	0	0	16	1	1	0	0	1
SME	5	0	0	0	0	0	0	0	0
Negative	184	94	2	152	35	158	101	90	140
% with carbapenemase	56.29	8.86	0.42	18.57	0.42	18.57	2.95	6.75	10.13
% KPC	87.76	10.10	0.48	12.02	0.00	20.19	3.37	7.69	10.58

Abbreviations: EPM, ertapenem; IMP, imipenem-hydrolyzing beta-lactamase; IPM, imipenem; KPC, ***Klebsiella pneumoniae*** carbapenemase; MER, meropenem; NDM, New-Delhi metallo-beta-lactamase; OXA, oxacillinase; S, susceptible; SME, ***Serratia marcescens*** enzyme.

Humphries RM. Clin Infect Dis. 2018 Mar 19;66(7):1061-1067.

ANTIMICROBIAL RESISTANCE & BREAKPOINTS

Antimicrobial resistance (AMR) is a global issue that threatens patient safety and public health

Key element to confront and manage AMR: detect & interpret resistance

Breakpoints are a moving target

Labs that do not apply up to date breakpoints impede global efforts to address AMR and adequately treat patients

CALL TO ACTION

A CALL TO ACTION: DEFINING THE PROBLEM

Open Forum Infectious Diseases

MAJOR ARTICLE

Raising the Bar: Improving Antimicrobial Resistance Detection by Clinical Laboratories by Ensuring Use of Current Breakpoints

Patricia J. Simner,[1] Carol A. Rauch,[2] Isabella W. Martin,[3] Kaede V. Sullivan,[4] Daniel Rhoads,[5] Robin Rolf,[6] Rosemary She,[7] Rhona J. Souers,[6] Christina Wojewoda,[8] and Romney M. Humphries[9]

[1]Johns Hopkins Medical Institute, Baltimore, Maryland, USA, [2]Vanderbilt University, Nashville, Tennessee, USA, [3]Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, USA, [4]Temple University Hospital, Philadelphia, Pennsylvania, USA, [5]Cleveland Clinic, Cleveland, Ohio, USA, [6]College of American Pathologists, Chicago, Illinois, USA, [7]University of Southern California, Los Angeles, California, USA, [8]University of Vermont Medical Center, Burlington, Vermont, USA, and [9]Vanderbilt University Medical Center, Nashville, Tennessee, USA

Between 29.5% and 62.1% of US labs reported using current breakpoints

55.9% indicated they did not have current plans to update

Open Forum Infect Dis. 2022 Feb 7;9(3):ofac007.

COLLEGE OF AMERICAN PATHOLOGISTS (CAP) 2024 BREAKPOINT REGULATION

- **New** MIC.11385 Current Antimicrobial Susceptibility Test Interpretation Breakpoints
  - “Effective January 1, 2024, the laboratory uses current breakpoints for interpretation of antimicrobial minimum inhibitory concentration (MIC) and disk diffusion test results and implements new breakpoints within three years of the date of official publication by the FDA or other standards development organization (SDO) used by the laboratory.”
- **Revised** MIC.11380 Antimicrobial Susceptibility Test Interpretation Criteria
  - “For antimicrobial susceptibility testing systems, there are written criteria for determining and interpreting minimal inhibitory concentration (MIC) or zone diameter sizes as susceptible, intermediate, resistant, non-susceptible, or susceptible dose-dependent. These criteria are reviewed annually.”

https://www.cap.org/laboratory-improvement/accreditation/accreditation-checklists

BREAKPOINTS: A US PERSPECTIVE

- **Problem**: Laboratories find it challenging to update breakpoints
  1. Unaware of breakpoint changes by CLSI and FDA
  2. Do not understand if they need to verify or validate new breakpoints
  3. Do not know how to audit breakpoints on cAST, breakpoint ranges not available on AST cards
- **bioMerieux's Goals**:
  - Create tools to inform VITEK2 users of breakpoint changes and approvals
  - Empower field application specialist team to support verification/validations
  - Reduce improper reporting of breakpoints and improve patient care

BIOMÉRIEUX
TOOLS & RESOURCES

VERIFICATION & VALIDATION GUIDES

PART 4 – SUMMARY OF RESULTS TEMPLATE

Table 3: Summary of Results

Drug	# of Isolates				CA		*EA		VME		ME		mE	
	Total	S	I	R	#	%	#	%	#	%	#	%	#	%

*Only required if drug has been reformulated

Discrepancy Resolution

Accuracy:

- Briefly describe how many discrepancies occurred for accuracy (Table 1). Isolates with a major error or very major errors should be repeated in triplicate. If errors persisted after repeat testing, describe how you attempted to resolve them (i.e., specimens were tested by an additional method such as disk diffusion or sent to a reference laboratory that has been verified for current breakpoints).

Precision (Reproducibility):

- Briefly describe how many discrepancies occurred for reproducibility (Table 2). Isolates with a major error or very major error should be repeated in triplicate. If errors persisted after repeat testing, describe how you attempted to resolve them (i.e., specimens were tested by an additional method such as disk diffusion or sent to a reference laboratory that has been verified for current breakpoints).

Reproducibility / Precision was performed on ___ number of isolates over ___ days.
The estimate for precision was ____.

Conclusions

This validation study demonstrates that the VITEK® 2 System provides accurate susceptibility interpretations utilizing the current MIC breakpoints for _____(insert drug name).

This validation study has been reviewed and is acceptable for patient testing.

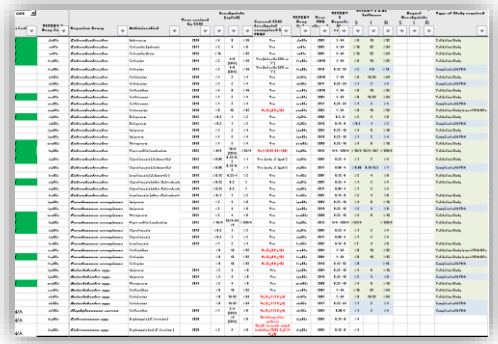
Reviewed by:
Date:
Signature:

BIOMÉRIEUX RESOURCES

Breakpoints Education: Internal & External

Series of three webinars to address individual needs of key stakeholders

VITEK® Breakpoint Audit Tool



Automated tool with CLSI, FDA & VITEK breakpoints

VITEK® Breakpoint Audit Tool Instructions

Instructions on efficient use of BAT

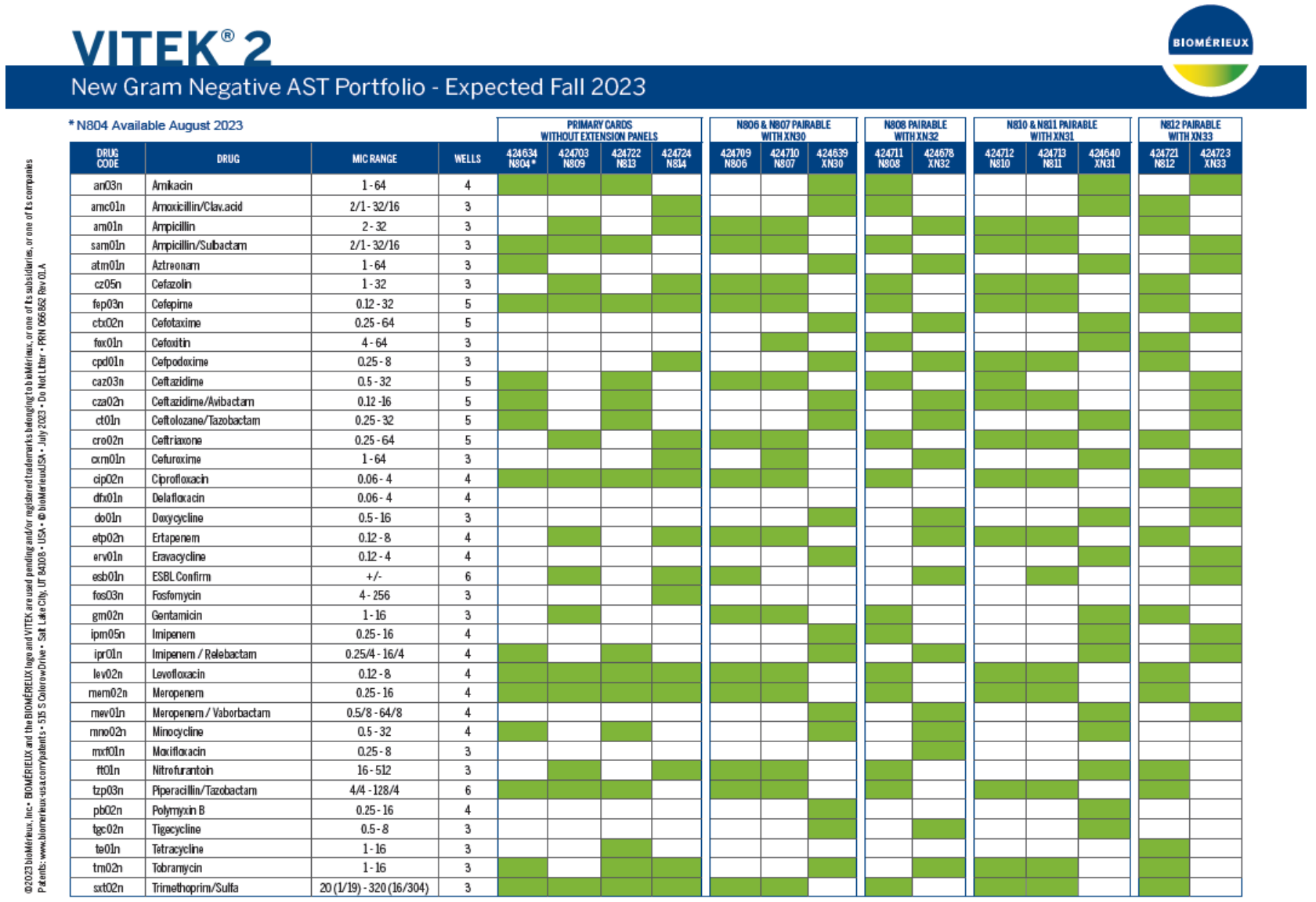
(Word & PowerPoint)

BREAKPOINT AUDIT TOOL (BAT)

- VITEK2 information: Card number, drug code,
- Breakpoints from VITEK, FDA, CLSI for each organism-antimicrobial combo
  - Includes year revised and agreement between CLSI & FDA
- Date of laboratory review
- Type of study required if breakpoints don't match

List	VITEK® 2 antibiotic version	Organism Group	Antimicrobial	Year revised by CLSI	CLSI MIC breakpoints			Current CLSI breakpoint recognized by FDA?	FDA STIC Hyper Link	VITEK® 2 antibiotic version	Year FDA cleared	VITEK® 2 Reportable range	VITEK® 2 9.02			AES User			Customer Breakpoint Matches CLSI? (Y / N)	Date Reviewed	Type of Study required if CLSI/FDA breakpoints do not match AES User Change Report Breakpoints?
					S	I	R						S	I	R	S	I	R			
1	am01n	*Enterobacterales*	Ampicillin	N/A	≤8	16	≥32	Yes	Ampicillin	am01n	<2010	2 - 32	≤8	16	≥32						Compliant
3	sam01n	*Enterobacterales*	Ampicillin / Sulbactam	N/A	≤8/4	16/8	≥32/16	Yes	Ampicillin and sulbactam	sam01n	<2010	2/1 - 32/16	≤8	16/8	≥32						Compliant
7	tzp03n	*Enterobacterales*	Piperacillin / Tazobactam	2022	≤8/4	16/4 (SDD)	≥32/4	No (<16 32-64 >128)	Piperacillin and tazobactam	tzp03n	2012	4/4 - 128/4	≤16/4	32/4 - 64/4	≥128/4						Validation study to meed CLSI BPs
8	cz01n	*Enterobacterales*	Cefazolin Systemic	2011	≤2	4	≥8	Yes	Cefazolin	cz01n	2001	4 - 64	≤16	32	≥64						N/A
8	cz01n	*Enterobacterales*	Cefazolin Urine	2016	≤16		≥32	Yes	Cefazolin	cz01n	2001	4 - 64	≤16	32	≥64						Validation study
9	fep02n	*Enterobacterales*	Cefepime	2014	≤2	4-8 (SDD)	≥16	Yes (but calls SDD an "I")	Cefepime	fep02n	<2010	1 - 64	≤8	16	≥32						Validation study
11	cro01n	*Enterobacterales*	Ceftriaxone	2010	≤1	2	≥4	Yes	Ceftriaxone	cro01n	2001	1 - 64	≤8	16-32	≥64						Validation study
13	fox01n	*Enterobacterales*	Cefoxitin	N/A	≤8	16	≥32	No (<4 8 >16)	Cefoxitin	fox01n	<2010	4 - 64	≤8	16	≥32						Validation Study to meet FDA BPs
15	caz01n	*Enterobacterales*	Ceftazidime	2010	≤4	8	≥16	Yes	Ceftazidime	caz01n	<2010	1 - 64	≤8	16	≥32						Validation study
18	etp01n	*Enterobacterales*	Ertapenem	2012	≤0.5	1	≥2	Yes	Ertapenem	etp01n	2004	0.5 - 8	≤2	4	≥8						Validation study
19	ipm04n	*Enterobacterales*	Imipenem	2010	≤1	2	≥4	Yes	Imipenem and cilastatin	ipm04n	2001	0.25 - 16	≤4	8	≥16						Validation study
21	gm01n	*Enterobacterales*	Gentamicin	2023	≤2	4	≥8	Yes	Gentamicin	gm01n	<2010	1 - 16	≤4	8	≥16						Validation Study
22	tm01n	*Enterobacterales*	Tobramycin	2023	≤2	4	≥8	Yes	Tobramycin	tm01n	<2010	1 - 16	≤4	8	≥16						Compliant
27	cip01n	*Enterobacterales*	Ciprofloxacin (other Enterobacterales)	2019	≤0.25	0.5	≥1	Yes	Ciprofloxacin	cip01n	2001	0.25 - 4	≤1	2	≥4						Validation study
27	cip01n	*Enterobacterales*	Ciprofloxacin (Salmonella)	2012	≤0.06	0.12-0.5	≥1	Yes (only S. typhi)	Ciprofloxacin	cip01n	2001	0.25 - 4	≤1	2	≥4						Validation study
28	lev02n	*Enterobacterales*	Levofloxacin (other Enterobacterales)	2019	≤0.5	1	≥2	Yes	Levofloxacin	lev02n	2007	0.12 - 8	≤2	4	≥8						Validation study
28	lev02n	*Enterobacterales*	Levofloxacin (Salmonella)	2013	≤0.12	0.25-1	≥2	Yes	Levofloxacin	lev02n	2007	0.12 - 8	≤2	4	≥8						Validation study
30	ft01n	*Enterobacterales*	Nitrofurantoin	N/A	≤32	64	≥128	Yes	Nitrofurantoin	ft01n	<2010	16 - 512	≤32	64	≥128						Compliant
30	sxt02n	*Enterobacterales*	Trimethoprim / Sulfamethoxazole	N/A	≤2/38		≥4/76	Yes	Trimethoprim and sulfamethoxa	sxt02n	<2010	20 (1/19) - 320 (16/304)	≤40		≥80						Compliant
6	fep02n	*P. aeruginosa*	Cefepime	N/A	≤8	16	≥32	No (S < 8 R > 16)	Cefepime	fep02n	<2010	1 - 64	≤8	16	≥32						Validation study to meet FDA BPs

VITEK2 CARD REFORMULATION: SELECTION GUIDE



VITEK® 2

New Gram Negative AST Portfolio - Expected Fall 2023

BIOMÉRIEUX

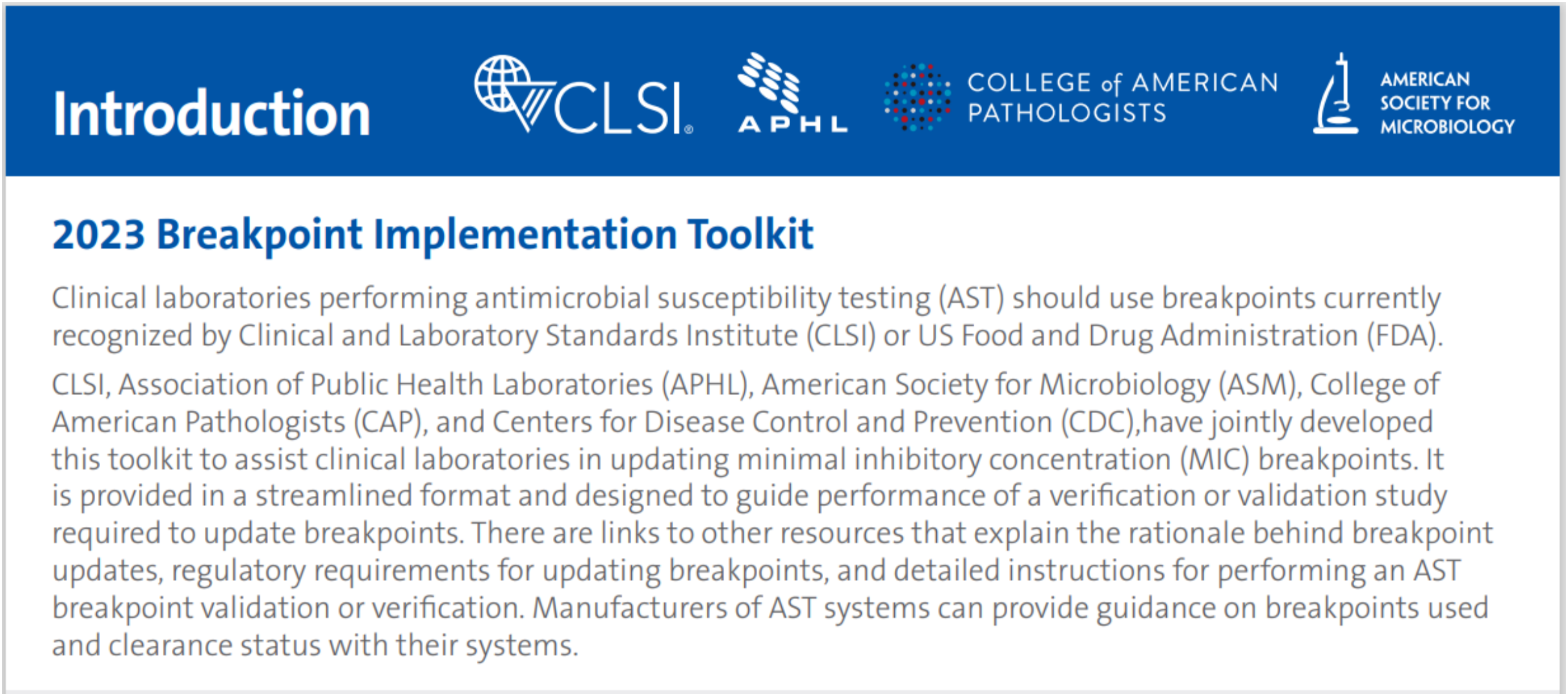
* N804 Available August 2023

				PRIMARY CARDS WITHOUT EXTENSION PANELS				N806 & N807 PAIRABLE WITH XN30			N808 PAIRABLE WITH XN32		N810 & N811 PAIRABLE WITH XN31			N812 PAIRABLE WITH XN33	
DRUG CODE	DRUG	MIC RANGE	WELLS	424634 N804*	424703 N809	424722 N813	424724 N814	424709 N806	424710 N807	424639 XN30	424711 N808	424678 XN32	424712 N810	424713 N811	424640 XN31	424721 N812	424723 XN33
an03n	Amikacin	1 - 64	4	■	■	■				■	■				■		■
amc01n	Amoxicillin/Clav.acid	2/1 - 32/16	3				■			■	■				■	■	
am01n	Ampicillin	2 - 32	3		■		■	■	■			■	■	■		■	
sam01n	Ampicillin/Subactam	2/1 - 32/16	3	■	■	■		■	■		■		■	■			■
atm01n	Aztreonam	1 - 64	3	■						■		■			■		■
cz05n	Cefazolin	1 - 32	3		■		■	■	■		■		■	■		■	
fep03n	Cefepime	0.12 - 32	5	■	■	■	■	■	■		■		■	■		■	
ctx02n	Cefotaxime	0.25 - 64	5							■		■			■		■
fox01n	Cefoxitin	4 - 64	3						■		■				■	■	
cpd01n	Cefpodoxime	0.25 - 8	3				■			■		■	■	■		■	
caz03n	Ceftazidime	0.5 - 32	5	■		■		■	■		■		■	■			■
cza02n	Ceftazidime/Avibactam	0.12 -16	5	■		■				■		■	■	■			■
ct01n	Ceftolozane/Tazobactam	0.25 - 32	5	■		■				■		■			■		■
cro02n	Ceftriaxone	0.25 - 64	5		■		■	■	■		■		■	■		■	
cxm01n	Cefuroxime	1 - 64	3				■		■			■			■		■
cip02n	Ciprofloxacin	0.06 - 4	4	■	■	■	■	■	■		■		■	■		■	
dfx01n	Delafloxacin	0.06 - 4	4														■
do01n	Doxycycline	0.5 - 16	3							■		■			■		■
etp02n	Ertapenem	0.12 - 8	4		■		■	■	■			■	■	■		■	
erv01n	Eravacycline	0.12 - 4	4							■		■			■		■
esb01n	ESBL Confirm	+/-	6		■		■	■				■		■			■
fos03n	Fosfomycin	4 - 256	3				■										
gm02n	Gentamicin	1 - 16	3		■			■	■		■				■	■	
ipm05n	Imipenem	0.25 - 16	4							■	■				■		■
ipr01n	Imipenem / Relebactam	0.25/4 - 16/4	4	■		■				■		■			■		■
lev02n	Levofloxacin	0.12 - 8	4	■	■	■	■	■	■		■		■	■		■	
mem02n	Meropenem	0.25 - 16	4	■	■	■	■	■	■		■		■	■		■	
mev01n	Meropenem / Vaborbactam	0.5/8 - 64/8	4							■		■			■		■
mno02n	Minocycline	0.5 - 32	4	■		■				■		■			■		
mxf01n	Moxifloxacin	0.25 - 8	3							■		■			■		
ft01n	Nitrofurantoin	16 - 512	3		■		■	■	■		■				■	■	
tzp03n	Piperacillin/Tazobactam	4/4 - 128/4	6	■	■	■		■	■		■		■	■		■	
pb02n	Polymyxin B	0.25 - 16	4							■					■		
tgc02n	Tigecycline	0.5 - 8	3							■		■			■		
te01n	Tetracycline	1 - 16	3			■										■	
tm02n	Tobramycin	1 - 16	3	■		■	■			■		■	■	■		■	
sxt02n	Trimethoprim/Sulfa	20 (1/19) - 320 (16/304)	3	■	■	■	■	■	■		■		■	■		■	

See your bioMérieux Representative for updates and questions.

TOOLS & RESOURCES

CLINICAL & LABORATORY STANDARDS INSTITUTE (CLSI)



https://clsi.org/media/qmeippiu/2023_breakpoint_implementation_toolkit.pdf

CLINICAL & LABORATORY STANDARDS INSTITUTE (CLSI)

- New edition of the M52 document (verification) under development
- Breakpoint Implementation Toolkit Webinar (October 2023)
- Updated CDC AR Bank organism sets
- M100 34th Edition (2024) → The updates never end!
  - Webinar April 17

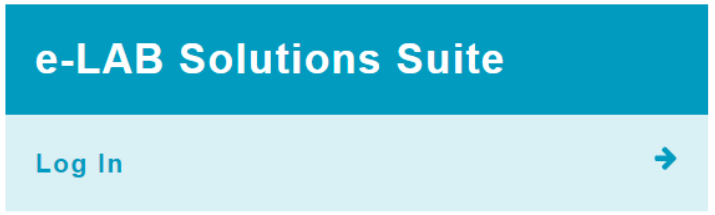
https://clsi.org/

COLLEGE OF AMERICAN PATHOLOGISTS (CAP)

e-LAB Solutions Suite

e-LAB Solutions Suite is our online portal to manage your laboratory improvement programs. The portal provides helpful, convenient, and easy-to-use tools to:

- Enter, review, and approve your PT results with interactive online forms.
- View and print copies of evaluations, participant summary reports, kit instructions, and result forms.
- Access your analyte scorecard, customized PT shipping calendar and other analytical tools.
- Connect to CAP Learning tools, assessments, and modules.
- Access user guides and PT Exception Investigation Checklist tools.
- Manage your laboratory's online access, user permissions, and your individual profile.
- Manage your laboratory's accreditation documents, including customized accreditation checklists and test menu/activity change forms.
- Enhance your automated reporting capabilities with e-LAB Solutions Connect and receive helpful email notifications (eg, if your proficiency testing data has not been received).



https://www.cap.org/laboratory-improvement/proficiency-testing/e-lab-solutions-suite

COLLEGE OF AMERICAN PATHOLOGISTS (CAP)

Be Prepared with These Resources from the CAP

To ensure our accredited laboratories are prepared for this new requirement, the CAP has the following resources available to help guide you through the transition.

Antimicrobial Susceptibility Testing: Understanding New CAP Requirements Module

This learning activity, presented by Romney Humphries, PhD D(ABMM), FAAM, FIDSA, provides expert insight into microbiology breakpoints, links to helpful resources, and knowledge checks to ensure understanding of the new requirements.

Complete the Activity

Breakpoint FAQs MIC.11380 and MIC.11385 Document

This document answers commonly asked question for updating breakpoints.

Review the FAQs

Updating Breakpoints in Antimicrobial Susceptibility Testing

Learn more about clinical breakpoints and the CAP's new checklist requirements in this American Society for Microbiology article.

Read the Article

https://info.cap.org/antimicrobial-susceptibility-testing/?

ASSOCIATION OF PUBLIC HEALTH LABORATORIES (APHL)

The CRO Breakpoint Implementation Toolkit

The AR Laboratory Workgroup identified providing assistance to laboratories in the implementation of updated carbapenem susceptibility breakpoints as an important area of work. To that end they developed a toolkit laboratories can utilize to guide them through the verification study needed to implement the updated breakpoints. **The first iteration of the toolkit focuses on updating carbapenem breakpoints for *Enterobacterales***. Future iterations will expand to include additional drug-bug combinations. The toolkit components include:

- Introduction to the CRO Breakpoint Implementation Toolkit
  A one-pager providing an overview of the necessity of updating breakpoints and the toolkit
- About the AR Isolate Bank
  A document containing frequently asked questions pertaining to ordering isolate panels for verification studies from the CDC & FDA Antibiotic Resistance (AR) Isolate Bank
- Verification Template
  A template laboratories can utilize for their verification study
- Breakpoint Implementation Instructions
  Step-by-step instructions for performing the verification study
- Implementation Worksheets
  Worksheet templates to be used in conjunction with isolates ordered from the AR Isolate Bank

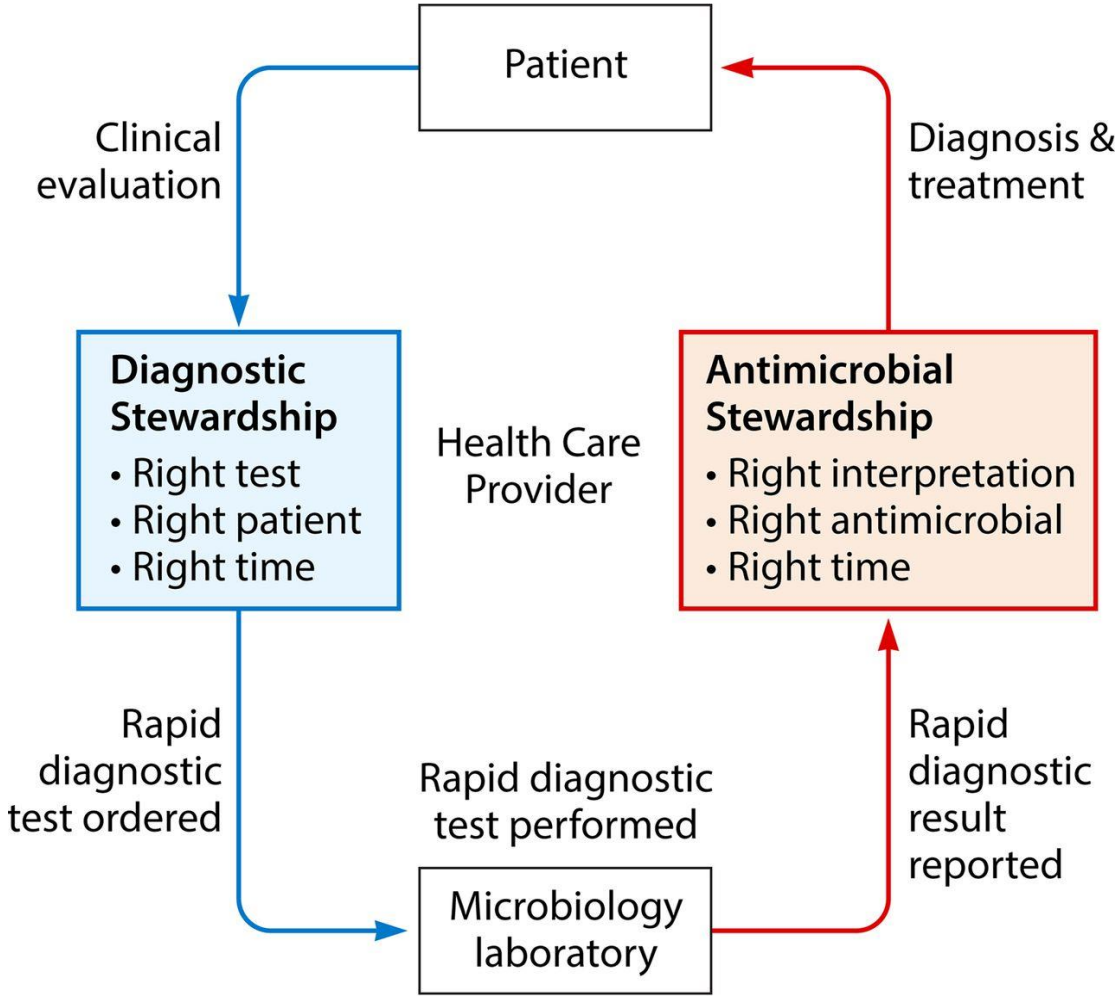
https://www.aphl.org/programs/infectious_disease/Pages/CRO-Breakpoint-Implementation-Toolkit.aspx

DIAGNOSTIC STEWARDSHIP FUNDAMENTALS

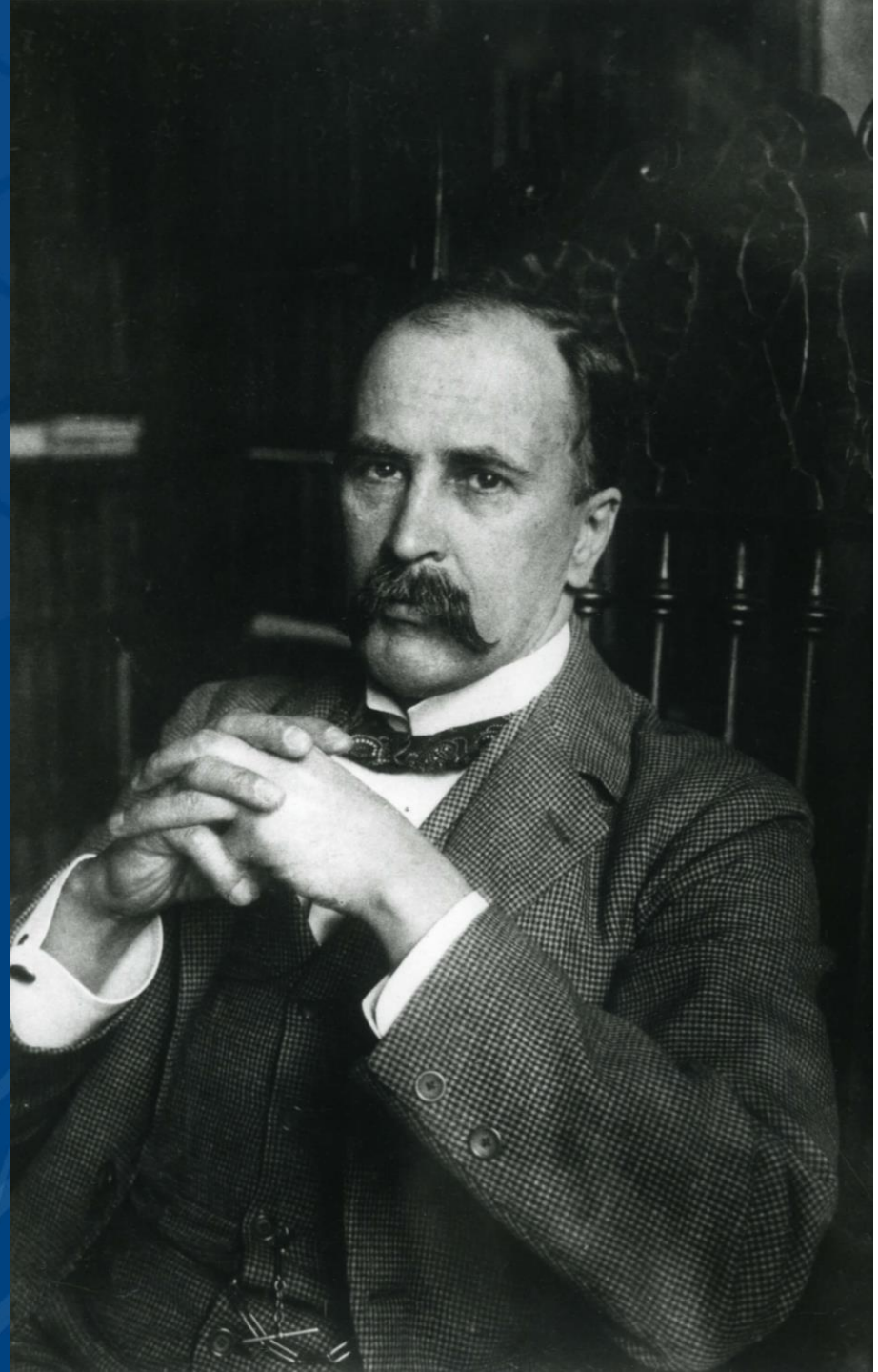
BIOMÉRIEUX

WHAT IS DIAGNOSTIC STEWARDSHIP

- **Right test**
- **Right patient**
- **Right time**
- **Right sample collection & handling**



Messacar K. J Clin Microbiol. 2017 Mar; 55(3): 715–723.



WHY DIAGNOSTIC STEWARDSHIP

- “Medicine is a science of uncertainty and an art of probability.” - William Osler (1849-1918)

- Diagnosing disease ≈ balancing probabilities

https://www.hopkinsmedicine.org/sebin/b/h/OSLER%20william.jpg

WHY DIAGNOSTIC STEWARDSHIP

- Common tests collected in patients without symptoms
  - *Clostridioides difficile*
  - Urine cultures
- Common syndromes prescribed antimicrobials without use of diagnostics
  - Respiratory cultures
- Leads to excessive antimicrobial use and other negative outcomes for patients

Morgan DJ. JAMA. 2017 Aug 15;318(7):607-608.

PRE-ANALYTICAL DIAGNOSTIC STEWARDSHIP

- Optimize test utilization
  - Clinician education
  - Test menu auditing
- Laboratory information system (LIS) & clinical decision support system (CDSS)
  - Benchmarking
  - Test utilization
- Specimen acceptability
  - Stool for *C. difficile* testing
  - Gram-stain screening for respiratory cultures

Hueth K. Antibiotics (Basel). 2022 Feb 15;11(2):250

POST-ANALYTICAL DIAGNOSTIC STEWARDSHIP

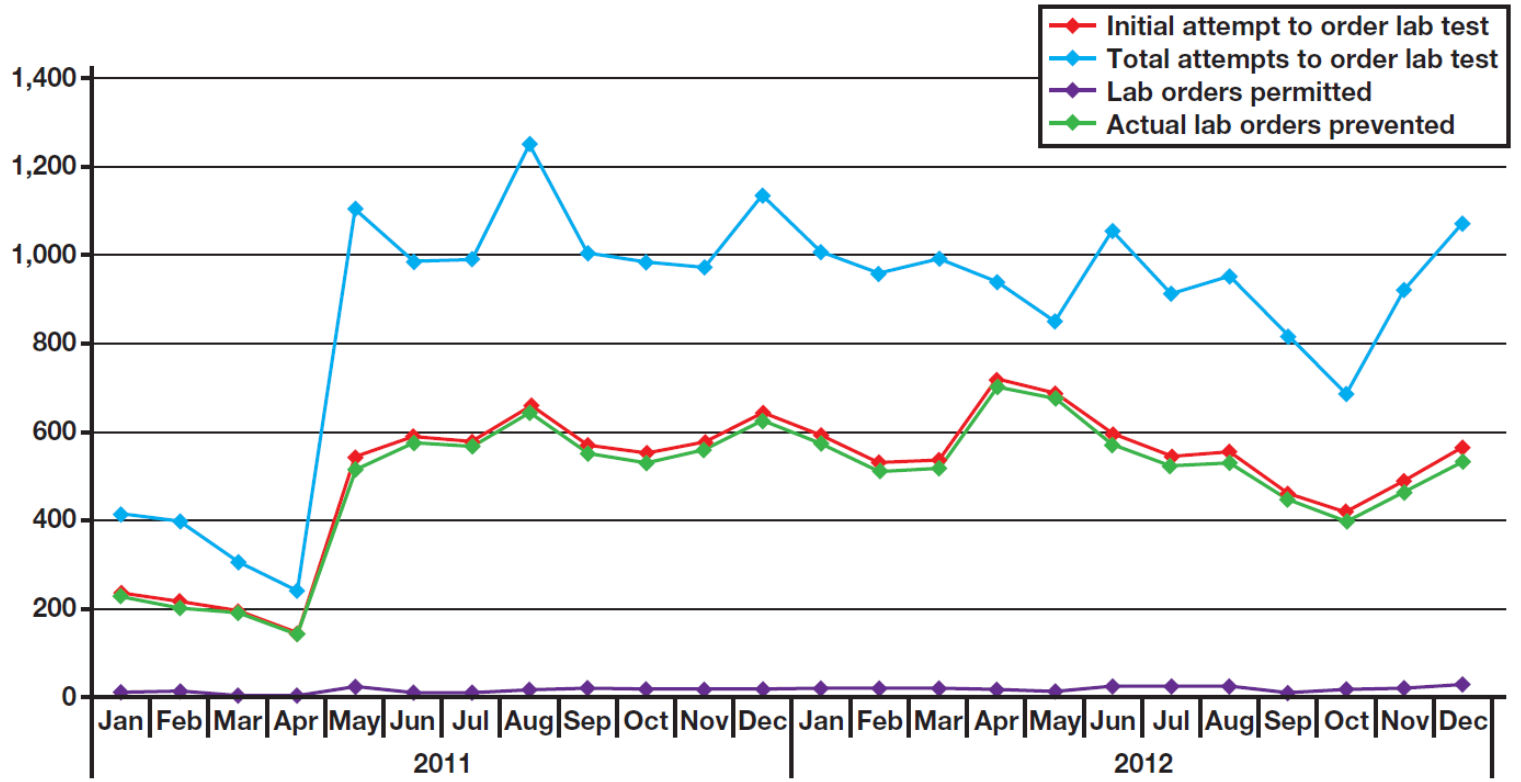
- Antimicrobial stewardship team prospective audit and feedback (PAF)
- Clinical decision support system
- Templated microbiology comments
- Local contextual factors (e.g., surgery service)
- Implementation and dissemination science

Hueth K. Antibiotics (Basel). 2022 Feb 15;11(2):250

DIAGNOSTIC STEWARDSHIP IN ACTION

PRE-ANALYTICAL DIAGNOSTIC STEWARDSHIP OUTCOMES

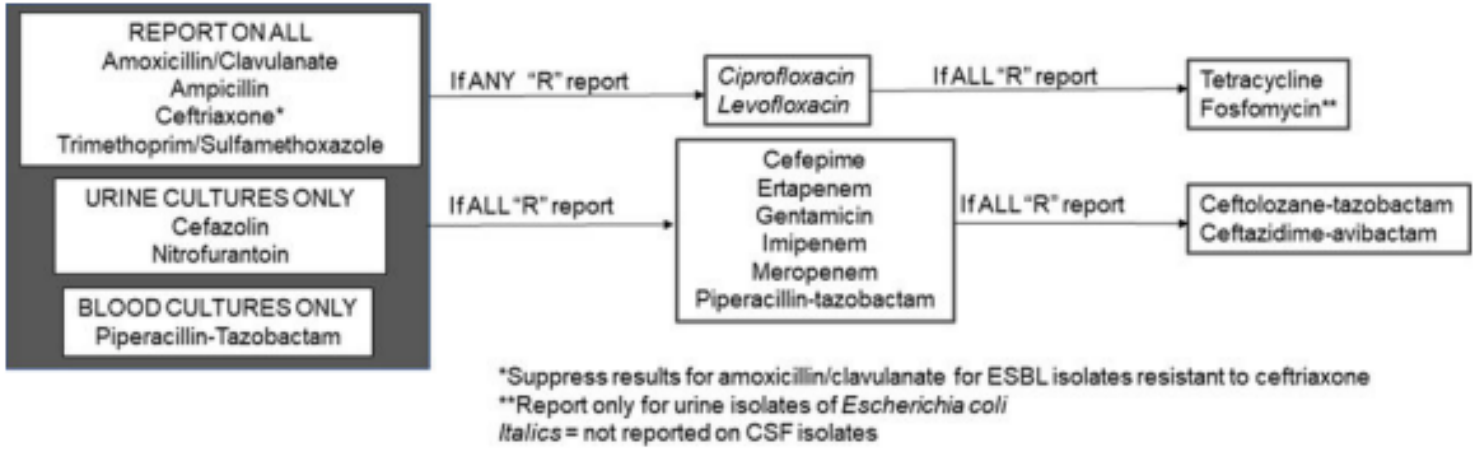
- Procop, et al. implemented a popup, hard stop alert for same-day duplicate orders in electronic healthcare system (EHR) for 1,259 lab orderables
- 12,204 initial duplicate test alerts were provided to clinicians
  - 11,790 duplicate tests were prevented (97%)
  - 414 duplicate tests were requested by phone (3%)



Procop GW. Am J Clin Pathol. 2014 May;141(5):718-23.

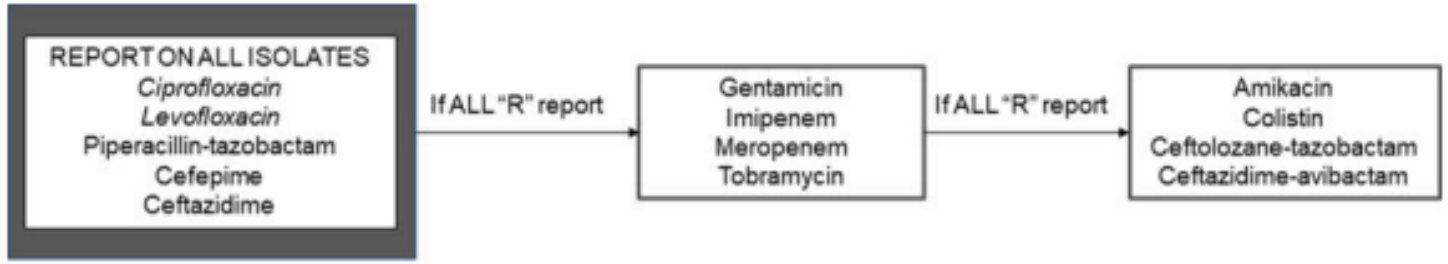
POST-ANALYTICAL DIAGNOSTIC STEWARDSHIP OUTCOMES

- Vissichelli, et al. implemented cascaded reporting for antimicrobials on Enterobacterales and *Pseudomonas aeruginosa* in 2018
- Enterobacterales



*Suppress results for amoxicillin/clavulanate for ESBL isolates resistant to ceftriaxone
**Report only for urine isolates of *Escherichia coli*
Italics = not reported on CSF isolates

- *P. aeruginosa*



Italics = not reported on CSF isolates

Vissichelli NC. Infect Control Hosp Epidemiol. 2022 Feb;43(2):199-204.

POST-ANALYTICAL DIAGNOSTIC STEWARDSHIP OUTCOMES

Consumption of Antimicrobials Before and After the Cascade Reporting Intervention

Outcome	Mean (SD) DOTs/1,000 DP During the Period Before the Intervention	Mean (SD) DOTs/1,000 DP During the Period After the Intervention	*P* Value
Amoxicillin/Clavulanate	13.86 (12.06)	20.23 (16.37)	.001
Cefpodoxime[a]	0.00 (0.00–0.00)	0.00 (0.00–0.00)	.065
Cephalexin	7.76 (9.08)	8.29 (10.18)	.702
Ciprofloxacin	18.38 (15.59)	16.53 (14.72)	.325
Levofloxacin	39.50 (26.64)	36.35 (24.75)	.362
Moxifloxacin[a]	0.00 (0.00–0.00)	0.00 (0.00–1.33)	.184
Trimethoprim/Sulfamethoxazole	10.15 (10.74)	10.76 (10.84)	.654
Ceftriaxone	30.41 (22.90)	28.27 (21.54)	.390
Cefepime	6.98 (10.12)	19.01 (20.09)	<.001
Meropenem	52.96 (43.83)	40.42 (32.97)	.005
Piperacillin/Tazobactam	132.56 (73.70)	113.80 (67.28)	.002

Note. SD, standard deviation; DOT, days of therapy, DP, days present.

[a]Median (interquartile range). The Wilcoxon signed-rank test was used due to low utilization.

Vissichelli NC. Infect Control Hosp Epidemiol. 2022 Feb;43(2):199-204.

TAKE HOME THOUGHTS

- It is vital to update breakpoints → supports global efforts to address AMR and adequately treat patients
- New CAP requirements present significant challenges for clinical laboratories
- bioMérieux is working on resources to help clinical laboratories address breakpoint challenges
- Diagnostic stewardship efforts can play a critical role in test volume, healthcare costs, and optimizing antibiotic use

ACKNOWLEDGEMENTS

Breakpoints Task Force

US Medical Affairs

Drs. Andrea Prinzi & Patrick McDaneld

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PIONEERING DIAGNOSTICS