Methods Development and Standardization Working Group Members:

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Methods Development and Standardization Working Group
June 3, 2018

Topic	Information
CoNS – WG Report	Vote
CLSI vs. EUCAST media – S. pneumoniae – WG Report	Vote
Susceptibility testing methods of ceftazidime-avibactam against susceptible and multidrug-resistant Gram-negative organisms	Vote
Colistin – WG Report	Vote
Coordinated Development – Drugs and Devices – WG Report	Information
Direct from Blood Culture AST - WG Report	Information

Coagulase-Negative *Staphylococcus* Species Oxacillin Resistance *ad hoc* Working Group (WG)

- Jennifer Dien Bard (co-Chair)
- Lars Westblade (co-Chair)
- Shelley Campeau
- Paul Edelstein
- Romney Humphries
- Jana Swenson

Background

- Laboratories are better able to identify Coagulase-negative *Staphylococcus* (CoNS) species to species level by MALDI-TOF MS
- Are current interpretive criteria for oxacillin against CoNS appropriate for contemporary isolates of S.epidermidis?

Current Breakpoints for Staphylococci – Table 2C

Organism	Oxacillin Breakpoint				Cefoxitin Breakpoint			
	DD (mm)		MIC (ug/ml)		DD (mm)		MIC (ug/ml)	
	S	R	S	R	S	R	S	R
S. aureus/S. lugdunensis	-	-	≤2	≥4	≥22	≤21	≤4	≥8
CoNS (except *S. lugdunensis*, *S. pseudintermedius*, *S. schlieferi)*	-	-	≤0.25	≥0.5	≥25	≤24	-	-
S. pseudintermedius, S. schlieferi	≥18	≤17	≤0.25	≥0.5	-	-	-	-

Study Plan

- Evaluate oxacillin and cefoxitin tests (disk diffusion [DD] and broth microdilution [BMD]) for detection of *mec*A-mediated beta-lactam resistance in *S. epidermidis*

- **Participating institutions for this data set:**
  - Children's Hospital Los Angeles (Jennifer Dien Bard, Samia Naccache)
  - Weill Cornell Medicine (Lars Westblade, Katrina Callan)
  - Washington University (Carey-Ann Burnham, Megan Wallace)

Isolates Included in Study

Institution	Quantity	Year	Specimen source
Children's Hospital Los Angeles (CHLA) Los Angeles, CA	40	2016-2018	Arterial line, CVC, PICC, peripheral blood
Weill Cornell Medicine (WCM) New York, NY	38	2016-2017	Peripheral blood, catheter
Washington University in Saint Louis (WUSTL) St. Louis, MO	22	2015, 2017	Blood, CSF, joint fluid, synovial fluid
Total	**100**		

mecA Distribution

Institution	*mecA* positive	*mecA* negative
CHLA	18	22
WCM	18	20
WUSTL	12	10
Total	**48**	**52**

Materials and Quality Control (QC)

- Broth microdilution (BMD): frozen-form panels (ThermoFisher) containing CA-MHB from 3 manufacturers:
  - Cefoxitin: 2-fold dilutions, 0.015-32 µg/mL
  - Oxacillin (2% NaCl): 2-fold dilutions, 0.015-32 µg/mL

- Disk diffusion (DD):
  - MHA from 3 manufacturers
  - Cefoxitin, 30 µg disk
  - Oxacillin, 1 µg disk

- PBP2a:
  - PBP2a SA Culture Colony Test (Alere)
  - PBP2′ Latex agglutination test (Oxoid)

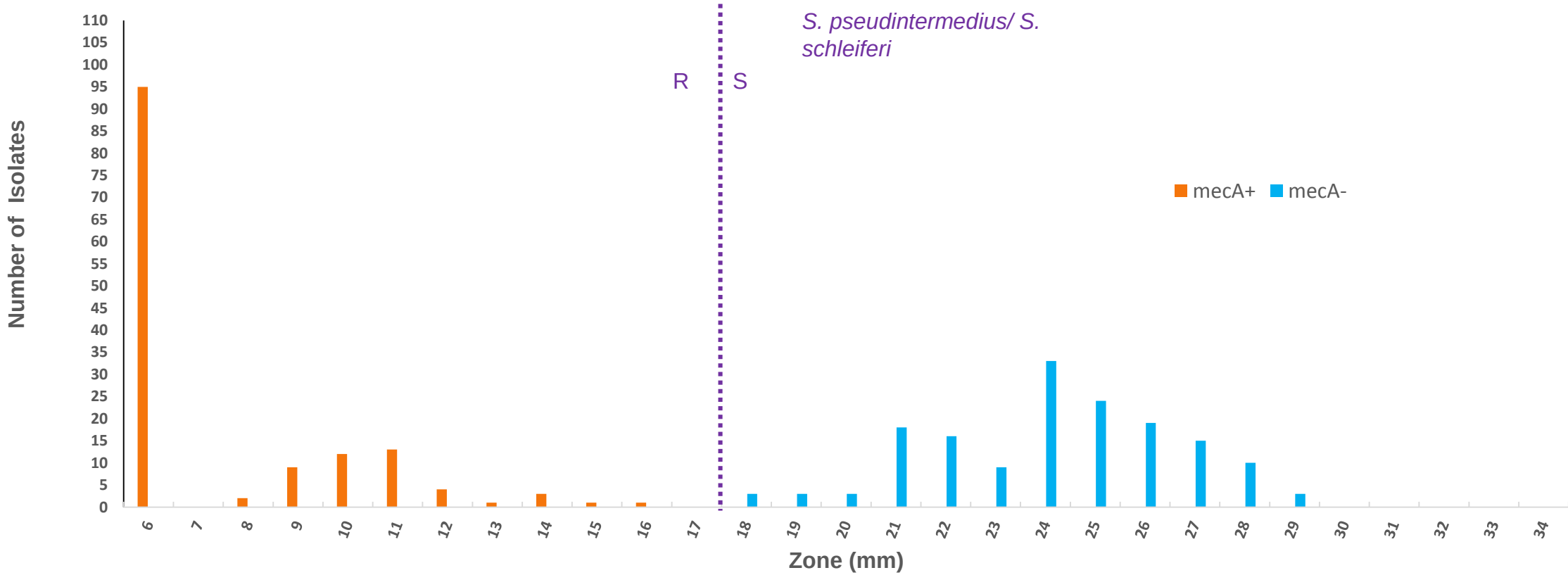
- QC:
  - BMD: *Staphylococcus aureus* ATCC® 29213
  - DD: *S. aureus* ATCC® 25923
  - PBP2a and PBP2′: *S. aureus* ATCC® 25923 and *S. aureus* ATCC® 43300

Performance of Cefoxitin DD for S. epidermidis showed current BPs for CoNS work

Method	M100-S28 Breakpoints	Breakpoints	CA	ME	VME
Cefoxitin DD	CoNS	S≥25;R≤24 (24h)	*100% 300/300*	*0% 0/156*	*0% 0/144*
	S. aureus / S. lugdunensis	S≥22;R≤21 (24h)	*97.7% 293/300*	*0% 0/156*	*4.9% 7/144*
Cefoxitin BMD	*S. aureus / S. lugdunensis*	S≤4;R≥8 (16-20h)	*96.2% 280/291*	*3.9% 6/153*	*3.6% 5/138*

Oxacillin Zone Size Distribution for S. epidermidis: All Media

N=297*



*one isolate with faint growth, no zone diameter reading

Performance of all DD and BMD Oxacillin Tests for S. epidermidis

Method	M100-S28 Breakpoints	Breakpoints	CA	ME	VME
Oxacillin DD	*S. pseudintermedius /S. schleiferi*	S≥18;R≤17 (16-18h)	*100% (297/297)*	*0% (0/156)*	*0% (0/141)*
Oxacillin BMD	*S. pseudintermedius /S. schleiferi* + CoNS	S≤0.25;R≥0.5 (24h)	*99.0% (288/291)*	*2.0% (3/153)*	*0% (0/138)*
	S. aureus /S. lugdunensis	S≤2;R≥4 (24h)	*90.8% (267/294)*	*2.0% (3/153)*	*17.0% (24/141)*

Conclusions

- Both oxacillin and cefoxitin disk diffusion interpreted by the following breakpoints reliably detected *mecA* positive and *mecA* negative *S. epidermidis* isolates:
  - Oxacillin disk diffusion interpreted by M100S 28th Ed. *S. pseudintermedius/ S. schlieferi* breakpoints. Categoric agreement (n=99) was 100%.
  - Cefoxitin disk diffusion interpreted by M100S 28th Ed. CoNS breakpoints. Categoric agreement (n=100) was 100%.
- Oxacillin MIC tests using recommended CoNS breakpoints yielded categoric agreement of 99% with 2% MEs and 0% VME.
- Vote to include oxacillin disk diffusion for *S. epidermidis* with the following breakpoints: (WG Vote 8-0-2)
  - S ≥ 18 mm; R = ≤17 mm

Modifications to Table 2C and to associated tables

Table 2C. *Staphylococcus* spp. (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	I	R	S	I	R	
PENICILLINASE-STABLE PENICILLINS (Continued)									
A	Oxacillin (For *S. pseudintermedius* and ***S. schleiferi***)	1 µg oxacillin	≥ 18		≤ 17	≤0.25	–	≥0.5	**(15)** Neither cefoxitin MIC nor cefoxitin disk tests are reliable for detecting *mecA*-mediated resistance in *S. pseudintermedius* and ***S. schleiferi.***
A	Oxacillin (For CoNS except *S. lugdunensis*, *S.*	–	–	–	–	≤0.25 (oxacillin)	–	≥0.5 (oxacillin)	**(16) *S. epidermidis*** **isolates with oxacillin MIC ≥0.5 µg/mL should be reported as oxacillin resistant. However, oxacillin MIC breakpoints may overcall resistance for**

Add S. epidermidis here

Comparison of CLSI and EUCAST Reference Media for *S. pneumoniae* Disk Diffusion

Background & Objective

- There are differences between the media recommended by CLSI and EUCAST for *S. pneumoniae* disk diffusion testing
- **Objective:** to determine whether these media differences impact susceptibility test results

- **CLSI recommended media:**
  - Mueller-Hinton agar supplemented with 5% Sheep blood
- **EUCAST recommended media:**
  - Mueller-Hinton agar supplemented with 5% mechanically defibrinated horse blood and β-NAD (20 mg/L)

Phase II Study Design

- To test 100 clinical *S. pneumoniae* isolates obtained from CDC bank
  - MHA+5% sheep blood and MH-F agar from BD
  - CDC *Streptococcus* panel from Trek

- **3 testing sites:**
  - CDC Streptococcus lab: Dr. Lesley McGee
  - Children's Hospital Los Angeles (CHLA): Dr. Jennifer Dien Bard
  - University of Rochester Medical Center: Dr. Dwight Hardy

Testing strategy

- Isolates sub-cultured from frozen, to BAP x 2
- A single 0.5 McFarland standard inoculum prepared, used for Disk diffusion (BD MHA and MH-F) and *Streptococcus* MIC panel
- QC using *S. pneumoniae* ATCC 49619 performed each day of testing.
- Used CLSI interpretive criteria

- All 3 sites used same lot of reagents, media, discs
- All 3 sites used the same QC organism sent to them by CDC

All Disk Diffusion Data Combined (using CLSI media as reference)

Antibiotic	20 hours				24 hours			
	%Categorical Agreement	%VME	%ME	% MiE	%Categorical Agreement	%VME	%ME	%MiE
Oxacillin	98.03	1.16	0.81	0	98.03	1.16	0.81	0
Ceftaroline	100	0	0	0	100	0	0	0
Vancomycin	99.66	0	0.34	0	99.66	0	0.34	0
Erythromycin	98.98	0	0	1.02	98.30	0	0	1.70
Doxycycline	98.30	1.6	0	1.02	97.38	1.6	0	1.02
Levofloxacin	98.31	0	0	1.69	98.31	0	0	1.69
Trim/sulfa	95.95	0	0	4.05	96.62	0	0	3.38
Clindamycin	96.18	1.79	0	2.03	98.01	0.89	0	1.01
Rifampin	100	0	0	0	100	0	0	0
Chloramphenicol	99.63	0	0.37	0	96.15	3.85	0	0
Quinupristin/dalfopristi	93.24	0	0	6.76	92.57	0	0	7.43
Linezolid	100	0	0	0	100	0	0	0

QC Data: No. of QC runs that passed

Drug (DD Reference Range, mm)	20 hours		24 hours		Isolates that failed QC	
	CLSI MHA+5% QC passed (%)	EUCAST MH-F QC passed (%)	CLSI MHA+5% QC passed (%)	EUCAST MH-F QC passed (%)	CLSI MHA+5% Range of zone diameter	EUCAST MH-F Range of zone diameter
Quinupristin/Dalfopristin (19-24)	22/30 (73.3%)	23/30 (76.7%)	22/30 (73.3%)	23/30 (76.7%)	25-28	25-28
Erythromycin (25-30)	29/30 (96.7%)	20/30 (66.7%)	30/30 (100%)	20/30 (66.7%)	31-32	32-36
Trimethoprim-sulfamethoxazole (20-28)	21/30 (70%)	30/30 (100%)	21/30 (70%)	30/30 (100%)	30-32	NA
Linezolid (25-34)	30/30 (100%)	25/30 (83.3%)	30/30 (100%)	25/30 (83.3%)	NA	35-36
Rifampin (25-30)	28/29 (96.6%)	26/29 (89.7%)	28/29 (96.6%)	25/29 (86.2%)	31	32-34
Oxacillin (</=12)	30/30 (100%)	29/30 (96.7%)	30/30 (100%)	29/30 (96.7%)	NA	13
Levofloxacin (24-31)	10/30 (33.3%)	19/30 (63.3%)	11/30 (36.7%)	19/30 (63.3%)	20-23	22-23
Clindamycin (19-25)	26/30 (86.7%)	23/30 (76.7%)	26/30 (86.7%)	23/30 (76.7%)	26	26-28
Doxycycline (25-34)	29/30 (96.7%)	27/30 (90%)	29/30 (96.7%)	27/30 (90%)	35	35-36
Chloramphenicol (23-27)	23/30 (76.7%)	22/30 (73.3%)	23/30 (76.7%)	20/29 (70.0%)	28-30	28-30
Vancomycin (20-27)	30/30 (100%)	26/30 (86.7%)	30/30 (100%)	26/30 (86.7%)	28	28
Ceftaroline (31-41)	24/30 (80%)	25/30 (83.3%)	24/30 (80%)	25/30 (83.3%)	42-44	42-46

QC Data by Site: No. of QC runs that passed, 20 hour read

Drug	CLSI MHA+5%			EUCAST MH-F		
	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
Quin/Dalfo	10/10 (100%)	2/10 (20%)	10/10 (100%)	10/10 (100%)	3/10 (30%)	10/10 (100%)
Erythromycin	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (0%)	10/10 (100%)
Trim/sulfa	10/10 (100%)	1/10 (10%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)
Linezolid	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	5/10 (50%)	10/10 (100%)
Rifampin	10/10 (100%)	9/10 (90%)	10/10 (100%)	9/9 (100%)	6/10 (60%)	10/10 (100%)
Oxacillin	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	9/10 (90%)	10/10 (100%)
Levofloxacin	7/10 (70%)	2/10 (20%)	1/10 (10%)	8/10 (80%)	6/10 (60%)	5/10 (50%)
Clindamycin	10/10 (100%)	6/10 (60%)	10/10 (100%)	10/10 (100%)	3/10 (30%)	10/10 (100%)
Doxycycline	10/10 (100%)	9/10 (90%)	10/10 (100%)	10/10 (100%)	7/10 (70%)	10/10 (100%)
Chloramphenicol	10/10 (100%)	4/10 (40%)	9/10 (90%)	9/9 (100%)	2/10 (20%)	10/10 (100%)
Vancomycin	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	6/10 (60%)	10/10 (100%)
Ceftaroline	10/10 (100%)	4/10 (40%)	10/10 (100%)	10/10 (100%)	6/10 (60%)	9/10 (90%)

QC Data by Site: No. of QC runs that passed, 24 hour read

Drug	CLSI MHA+5%			EUCAST MH-F		
	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
Quinupristin/Dalfopristin	10/10 (100%)	2/10 (20%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)
Erythromycin	9/10 (90%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	0/10 (0%)	10/10 (100%)
Trimethoprim-sulfamethoxazole	10/10 (100%)	1/10 (10%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)
Linezolid	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	5/10 (50%)	10/10 (100%)
Rifampin	10/10 (100%)	9/10 (90%)	10/10 (100%)	8/9 (88.9%)	6/10 (60%)	10/10 (100%)
Oxacillin	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)
Levofloxacin	8/10 (80%)	2/10 (20%)	1/10 (10%)	8/10 (80%)	6/10 (60%)	5/10 (50%)
Clindamycin	10/10 (100%)	6/10 (60%)	10/10 (100%)	10/10 (100%)	3/10 (30%)	10/10 (100%)
Doxycycline	10/10 (100%)	9/10 (90%)	10/10 (100%)	10/10 (100%)	7/10 (70%)	10/10 (100%)
Chloramphenicol	10/10 (100%)	4/10 (40%)	9/10 (90%)	8/9 (88.9%)	2/10 (20%)	10/10 (100%)
Vancomycin	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	6/10 (60%)	10/10 (100%)
Ceftaroline	10/10 (100%)	4/10 (40%)	10/10 (100%)	10/10 (100%)	6/10 (60%)	9/10 (90%)

Conclusions:

- CLSI media and EUCAST media for DD testing of S. pneumoniae yield equivalent results, pending investigation of QC results. (At WG, QC data by site were not available.) WG Vote 9-0-1

- **CLSI recommended media:**
  - Mueller-Hinton agar supplemented with 5% Sheep blood
- **EUCAST recommended media:**
  - Mueller-Hinton agar supplemented with 5% mechanically defibrinated horse blood and β-NAD (20 mg/L)

Ceftazidime-avibactam disk breakpoints

Eric Wenzler, PharmD, BCPS, AAHIVP

Current CLSI-approved Breakpoints for Ceftazidime/Avibactam

- BMD MIC Breakpoints
  - Susceptible ≤8/4 mcg/ml
  - Resistant ≥16 mcg/ml
- Disk Diffusion Breakpoints
  - Susceptible ≥21 mm
  - Resistant ≤20 mm

Objective of the Presentation

- To determine the correlation of the current disk diffusion breakpoints with MIC breakpoints using various data sets

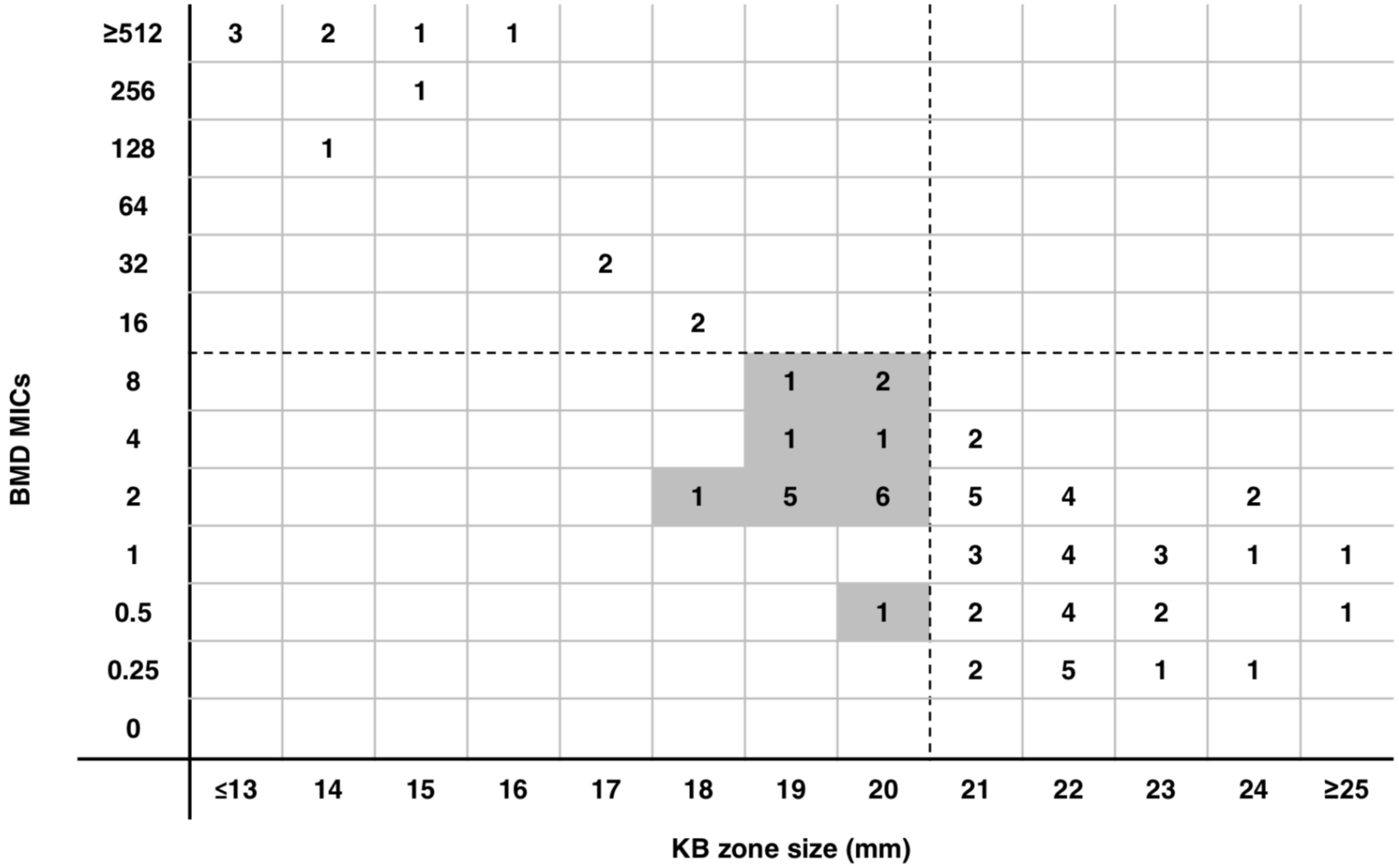
Data Sets for the Analysis

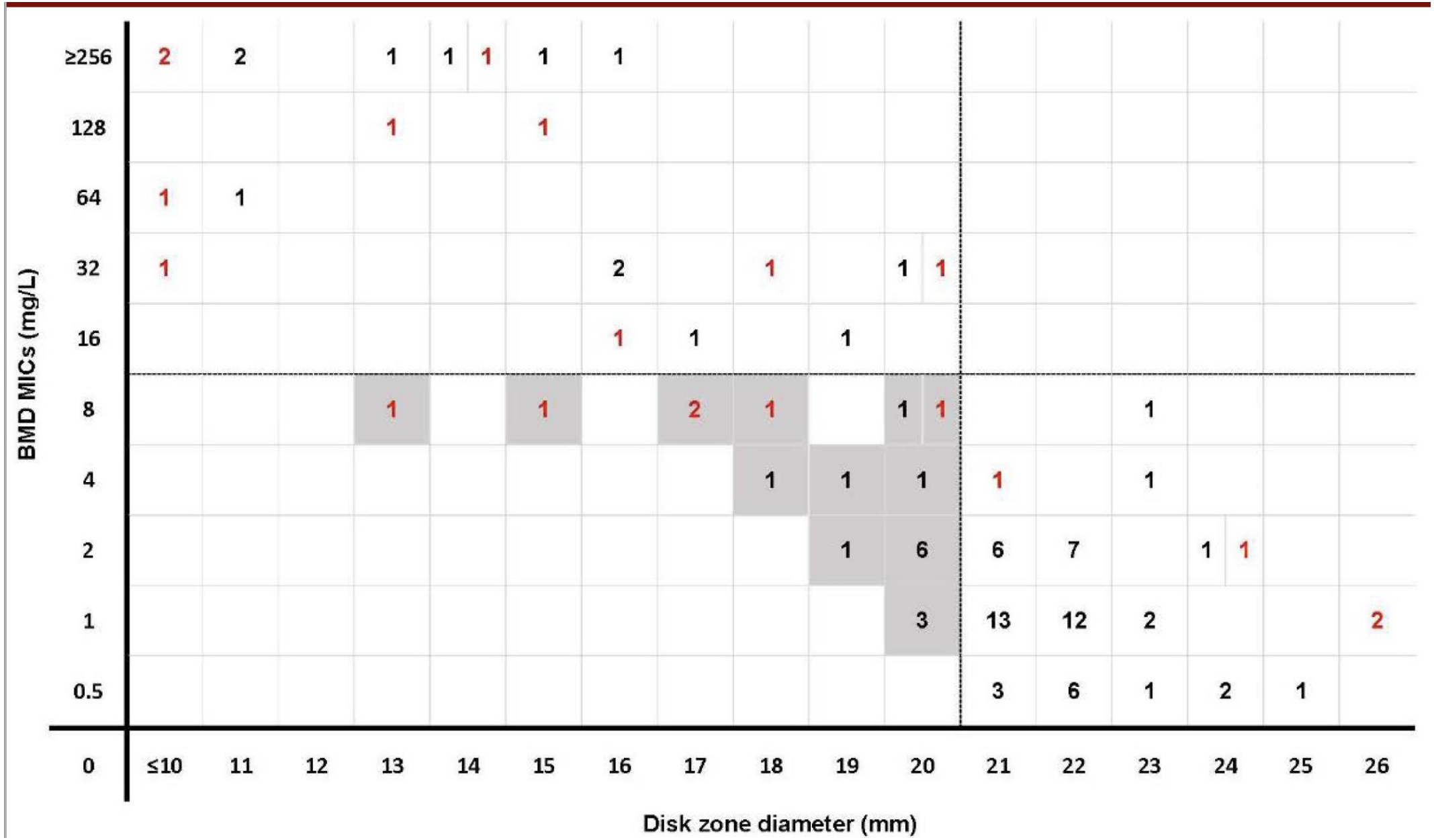
512 (476 Enterobacteriaceae, 56 P. aeruginosa) from NDA submission

- 74 CRE (Shields et al JCM) 76% CA; 29.5% ME; 0% VME
- 102 GNR
  - 69 meropenem/ ceftazidime-R K. pneumoniae
  - 20 P. aeruginosa (2 VIM, 2 IMP)
  - 13 non-K. pneumoniae, MDR

Wenzler study:
80.4% CA
25.0% ME
0.0% VME

Shields et al (JCM)





Wenzler et al (agenda book) – both Enterobacteriaceae and P.aeruginosa (red)

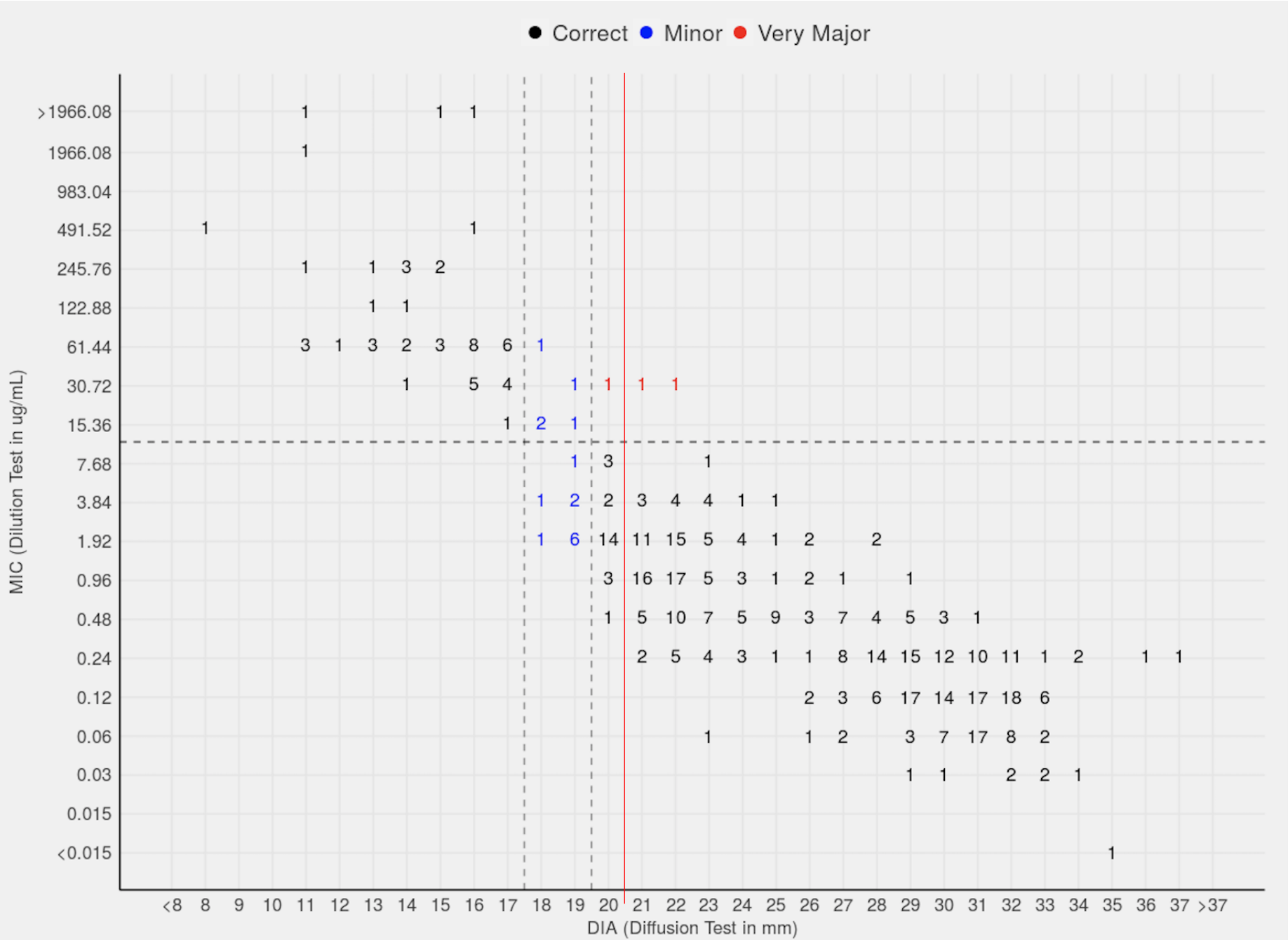
Combination with data from NDA (Enterobacteriaceae):

2 VME (3.3%)
34 ME (8.2%)

Challenge:
NDA enriched with isolates that would not likely be tested vs. CZA

dBETs software:
(17/18-19/20 mm):

3 VME (5%)
0 ME (0%)
16 mE (3%)

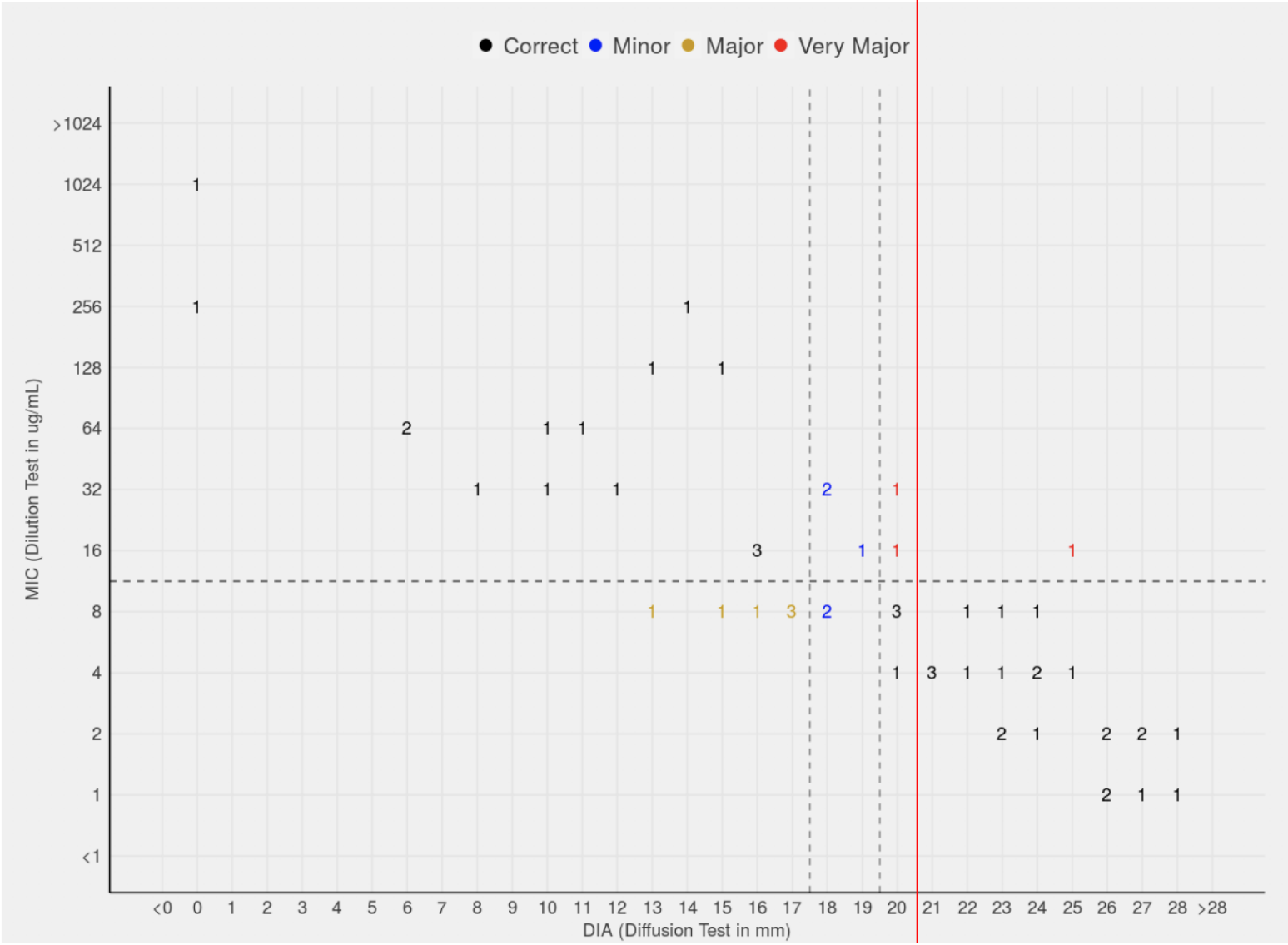


P. aeruginosa: NDA + Wenzler

12 ME (34%)
1 VME (4.7%)

dBETs:

3 VME (14%)
6 ME (17%)
5 mE (9%)



Discussion from ahWG

- Propose to modify disk diffusion breakpoints as follows:
  - **Susceptible ≥20 mm**
  - **Intermediate 18-19 mm**
  - **Resistant ≤17 mm**
- Concern that the intent of “I” by disk might be confusing (dose). Suggestion to add a comment
  - **“Isolates with zones of 18-19 mm may test susceptible by MIC, confirmatory testing is indicated.”**

AST Methods for Colistin

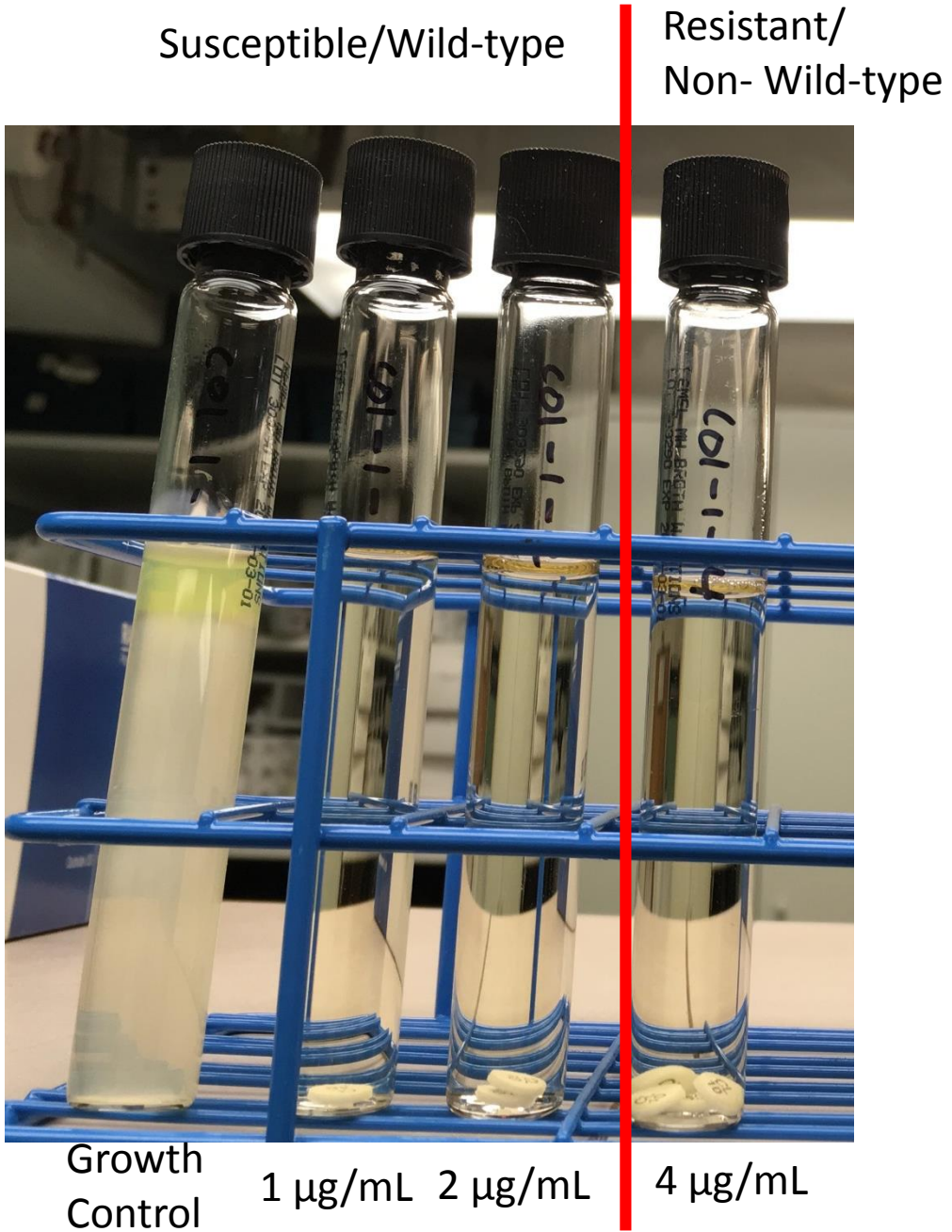
Colistin ad hoc WG

Review of ahWG

- NO practical method for colistin testing in clinical labs
- Updates:
  - Deleted disk breakpoints
  - Comment to not use gradient diffusion
  - Breakpoints for P. aeruginosa, Acinetobacter spp.
    - Rationale document submitted to FDA
  - Allow testing of colistin to predict polymyxin B
- Data presented:
  - JHU/UCLA (Trish Simner)
    - Colistin Broth Disk-Elution (CBDE) method for determining colistin MICs
    - eCBDE (EDTA-CBDE method) – not to be discussed, prelim data only
    - Broth macrodilution – not to be discussed, prelim data only
  - Mayo Clinic (Audrey Schuetz)
    - Agar dilution – work ongoing
    - Polymyxin NP – not to be discussed, impractical

Colistin Broth Disk-Elution (CBDE) Method

- Add 0 (growth control), 1, 2, and 4 colistin disks (10 µg; BD) to four 10 mL CA-MHB (Remel)
- Incubate tubes for 30 mins
- Add 50 µL of a 0.5 McFarland inoculum
- Vortex
- Incubate 18-20 hours at 35˚C
- Visually read MICs



Two-Site Evaluation- CBDE

Microbe Late-Breaker: SATURDAY-CPHM-LB3

Isolates	N	BMD Results		CA (%)	EA (%)	VME (%)	ME (%)
		S or WT (N)	R or NWT (N)				
Site 1 - UCLA							
A. baumannii	12	5	7	100	100	0	0
P. aeruginosa	20	18	2	100	100	0	0
Enterobacteriaceae	24	10	14	100	100	0	0
Site 2 - JH							
Retrospective CRE	65	58	7	100	97[a]	0	0
A. baumannii	12	12	0	100	100	0	0
P. aeruginosa	14	14	0	100	100	0	0
Enterobacteriaceae	19	17	2	100	100	0	0
Both Sites (UCLA and JH)							
mcr-1 E. coli[b]	6	0	6	50	100	50	0
Overall							
GNB	172	134	38	98	99	8	0

[a] 1 *C. freundii* had a MIC of ≤0.25 µg/mL by BMD and 2 µg/mL by CBDE and 1 *E. cloacae* had a MIC of 0.5 µg/mL by BMD and 2 µg/mL CBDE

[b] 3 *mcr-1 E. coli* had MICs of 2 µg/mL by CBDE and 4 µg/mL by BMD. These results were reproduced at the 2 sites.

Reproducibility Testing – *mcr-1* producing *E. coli*

All methods setup on the same day from the same sub-culture

CDC AR Bank #	CDC Result (µg/mL)	Broth Microdilution (µg/mL)				Colistin Broth Disk-Elution (µg/mL)			
		Day 1	Day 2	Day 3	Mode	Day 1	Day 2	Day 3	Mode
AR346	4	4	≥8	≥8	≥8	4	4	4	4
AR349*	2-4	2	4	4	4	2	4	4	4
AR350*	4	2	4	4	4	4	4	4	4
AR493	8	≥8	≥8	≥8	≥8	4	4	4	4
AR494	8	≥8	≥8	≥8	≥8	4	4	4	4
AR495*	4	4	4	4	4	4	4	4	4

* Isolates that demonstrated MIC of 2 µg/mL by CBDE on initial testing at both sites.

Vote at WG

- MDR GNR infections and lack of a readily available practical test to detect Colistin resistance constitutes a public health emergency
- Provisional vote of CBDE AS SCREENING method for M100-S29
  - Excluding *E. cloacae*
  - *Comment that isolates with MIC >1 ug/mL should be confirmed*
    - *mcr-1* test and/or BMD MIC
  - Pending confirmation of QC strain (NCTC 13846)
  - Vote 9-0-1

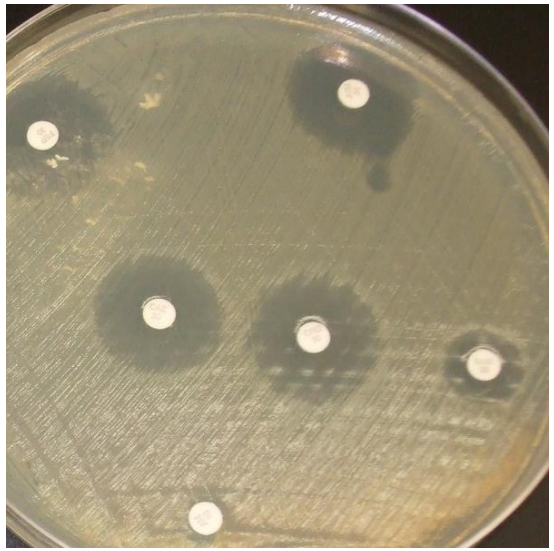
- 3 lab study to further confirm method:
  - CBDE (2 lots CA-MHB), BMD (3 lots CA-MHB), AD (2 lots MHA)
  - 100 Enterobacteriaceae, 50 A. baumannii, 50 P. aeruginosa
  - *A priori* plan to evaluate discrepancies
    - eCBDE for mcr detection, TDS (1 site)

Direct Blood Culture AST *Ad hoc* Working Group

Shelley Campeau, Co-chair

Audrey Schuetz, Co-chair

April Bobenchik, Recording Secretary



Eileen Burd

Dwight Hardy

Romney Humphries

Kristie Johnson

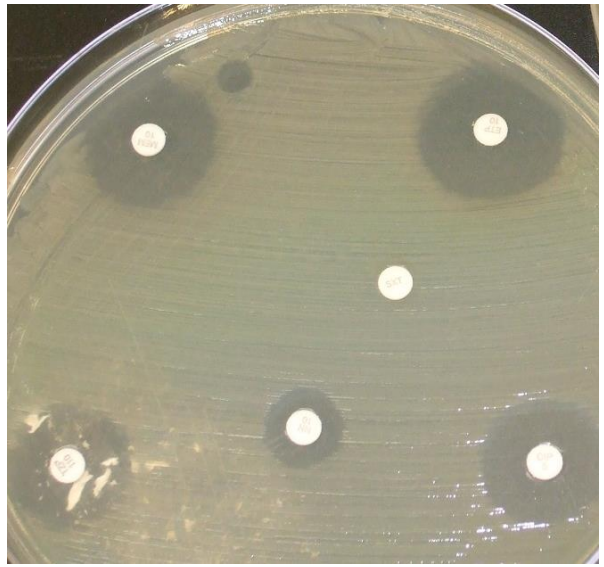
Tom Kirn

Dyan Luper

Robin Patel

Lauri Thrupp

Mel Weinstein



Background

- Multicenter study assessing disk diffusion direct from positive blood culture bottles for Gram-negative bacteria
- Antibacterial Resistance Leadership Group (ARLG) funding was secured last year
  - Funded by NIAID/NIH and facilitated by Duke Clinical Research Institute (DCRI)
  - Mission of ARLG: to prioritize, design and execute clinical research that will reduce the public health threat of antibacterial resistance
- Study design presented at past meetings

Hypothesis and Outcome Measures

- Direct-from-blood culture DD test read at 16-18 hrs performs at or above CLSI standards* as compared to standard DD and to reference BMD
- Direct-from-blood culture DD test read at 8-10 hrs performs at or above CLSI standards as compared to standard DD and to reference BMD

*CLSI M52

Study Progress

As of 5/22/2018

- All 5 sites have been activated
- Site enrollment numbers:
  - Site A: 31
  - Site B: 50
  - Site C: 75
  - Site D: 30
  - Site E: 103 (completed enrollment 5/21/18; final data review expected within next 2 weeks)
- 18/289 (6.2%) excluded to date
  - Mixed GNR + GP; GN anaerobes
- Bactec, BacTAlert, Thermofisher VersaTrek represented

Study Updates

- Challenges at some sites
  - Low enrollment numbers with at least 2 sites not expected to make the 100 mark/site
  - Enrolling within 8 hours of flagging positive
  - Occasional QC out of range
  - Reading disk results within time frame
- Removed 20 isolate restriction for *E. coli* at sites that perform rapid identification methods
  - There is now no restriction on number of *E. coli*
  - Workflow issues for labs who were waiting for rapid identification to rule out *E. coli*
- Based on current enrollment, projected to reach approximately 420 isolates for all sites
  - Working with sites to encourage training as many technologists as possible to set up and perform reading of disks
  - Expanding hours during which enrollment can occur

Timeline

- Last patient in: 8/1/2018
- Database lock: 9/1/2018
- Draft of paper/report: 11/15/2018

- Direct Blood Culture AST working group will meet in the fall of 2018 to discuss data
- Final report from ARLG DISK trial will be presented at January 2019 CLSI meeting