

External Quality Assessment

in Antimicrobial Susceptibility testing and in screening for multiresistant organisms

Performance 2018

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Performance 2018

Antimicrobial susceptibility testing UKNEQAS highlights – Annika Carlsson Wistedt

Antimicrobial susceptibility testing EARS-Net highlights - Barbara Holzkecht

Screening for multiresistant organisms - MRSA, VRE, ESBL and Carbapenemases – Kaisu Rantakokko-Jalava

How to use the results for improvement in the laboratory – Lise Hulløen-Orø

External Quality Assessment

in Antimicrobial Susceptibility testing and screening for multiresistant organisms

Frequently used schemes:

AST

UKNEQAS Antimicrobial susceptibility testing	12 x 2 isolates
EARS-Net	1 x 6 isolates
Labquality integrated in detection/identification	several
Folkehelseinstituttet Bact EQA (Norway)	4 times/year

Screening for multiresistant organisms

UKNEQAS MRSA	4x2 samples
EQUALIS MRSA	4x5-6 samples
EQUALIS VRE	4x5-6 samples
Labquality MRSA	4x1 sample
Labquality VRE	4x1 sample
Labquality MDR Gram-negative rods	4x1 sample

UKNEQAS Antimicrobial susceptibility testing

Approximate number of participating laboratories 2018:

500 (430 "EUCAST", 70 "CLSI")



21



17



12



14



1

UKNEQAS Antimicrobial susceptibility testing

Approximate number of participating laboratories 2018:

500 (430 "EUCAST", 70 "CLSI")



21



17



12



14



1



Staphylococci

Isolate	Species	Pattern/ Resistance
4480	S.aureus	MSSA, R: iCLI, MUP, PCV
4612	S.aureus	MSSA, R: iCLI, PCV
4704	S.aureus	MRSA, R: CLI CIP, GEN, RIF
4132	S.haemolyticus	R: OXA, CIP, iCLI, FUS, GEN, MUP, TEI, TET

Overall good performance

- Some still confused about inducible/ **dissociated** clindamycin resistance
- Oxacillin testing is not recommended – discordant results for one MSSA

Staphylococci-inducible/ *dissociated* clindamycin resistance report "R"

***EUCAST*: If** Inducible clindamycin resistance can be detected, then **report as resistant** and adding this comment to the report:

Staphylococci: "Clindamycin **may still be used for short-term** therapy of less serious skin and soft tissue infections as constitutive resistance is unlikely to develop during such therapy".

Streptococci "Clindamycin **may still be used for short-term** therapy of less serious skin and soft tissue infections as constitutive resistance is unlikely to develop during such therapy". The clinical importance of inducible clindamycin resistance in combination treatment of severe *S. pyogenes* infections is not known.



Staphylococci - oxacillin

Table 2: Cefoxitin and Oxacillin reports for *S. aureus*, specimen 4480.

Guideline	Method	n (%*) of participants reporting					
		Cefoxitin			Oxacillin		
		S (%)	I (%)	R (%)	S (%)	I (%)	R (%)
EUCAST/ EUCAST- related	Automated	106 (78.5)	0 (0.0)	29 (21.5)	95 (45.5)	0 (0.0)	114 (54.5)
	Disk diffusion	233 (97.9)	0 (0.0)	5 (2.1)	36 (81.8)	0 (0.0)	8 (18.2)
	MIC	13 (92.9)	0 (0.0)	1 (7.1)	32 (78.0)	1 (2.4)	8 (19.5)
	Multi/other	31 (93.9)	0 (0.0)	2 (6.1)	16 (55.2)	0 (0.0)	13 (44.8)
	Total	383 (91.2)	0 (0.0)	37 (8.8)	179 (55.4)	1 (0.3)	143 (44.3)

EUCAST table: Occasionally oxacillin MIC values are high in *S. aureus* in absence of *mec*-gene mediated resistance. These strains have been called BORSA (borderline oxacillin resistant *S. aureus*). EUCAST does not recommend systematic screening for BORSA.

Streptococci

Isolate	Species	Pattern/ Resistance
4430	S.pneumoniae	R: PCG 2-4, I: CTX 2-1
4392	Beta-hemolytic gG strept	R: iCLI, ERY
4572	Beta-hemolytic gG strept	R: iCLI, ERY, TET

- Poor agreement on borderline cefotaxime and penicillin S.pneumoniae
- Some still confused about inducible/ *dissociated* clindamycin resistance.

Enterococci

Isolate	Species	Pattern/ Resistance
4178	E.faecalis	VRE, <i>vanA</i>
4528	E.faecium	GenHLR pos, R: AMP

Overall good performance

- Some incorrect reports on Gentamicin-HLR (High Level Resistance) both ways.
- No VanB challenge this year

Enterobacteriales

Isolate	Species	Pattern/ Resistance	Mechanism/s
4347	E.coli	R. AMP, AMC	TEM-1
4179	E.coli	pAmpC/ ESBL-M R: ETP, PTZ	<i>bla</i> CMY-2 + porin loss
4391	E.coli	ESBL-A, R: AMI, GEN, TOB	TEM-1, ESBL CTX-M-15,OXA-1
4527	K.pneumoniae	ESBL-A, I: AMI, R: PTZ, AMC , GEN, TOB	<i>bla</i> SHV-5, aacA1, aacA4
4227	K.pneumoniae	CPE/ ESBL-CARBA I: MER, CTX	TEM-1, OXA-48
4431	K.pneumoniae	CPE/ESBL-CARBA, R: MER , CTX, GEN, TOB	TEM-1, IMP-1,OXA-2
4571	E.cloacae	CPE/ ESBL-CARBA, R: IMI , AMI, CIP, GEN, TIG, TOB	TEM-1, CTX-M-15,OXA-1, CMY NDM-1

- Good performance on detection of ESBL and Carbapenems
- Problems when levels of resistance (S/ I /R) in affected betalactams are reported

Enterobacterales and piperacillin-tazobactam I

4179 *E. coli* pAmpC/ ESBL-M (CMY2)
 Breakpoints: S ≤ 8 R > 16 mg/L S ≥ 20 R < 17 mm

Reference labs: PTZ MIC ≥ 128, ≥ 128 **Resistant**
 ATU= I : 16mg/L ; 17-19mm

	Piperacillin-tazobactam			% concordance
	S	I	R	
SE	0	0	22	
NO	0	1	16	
DK	0	3	8	
FI	2	3	12	
EUCAST	32	70	388	79,2%

ATU+ "I"

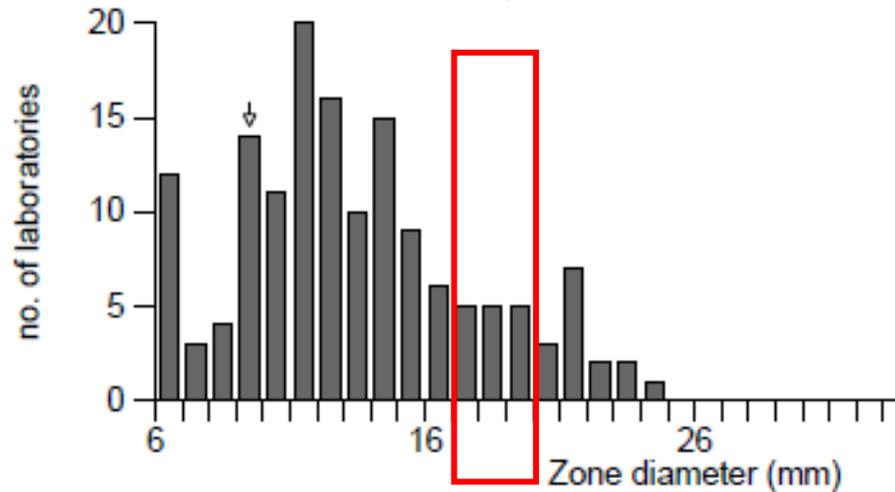


Table 2: Piperacillin-tazobactam resistance reports for *E. coli*, specimen 4179.

Guideline	Method	n (%*) of participants reporting		
		S (%)	I (%)	R (%)
EUCAST/EUCAST-related	Automated	9 (3.6)	55 (21.7)	189 (74.7)
	Disk diffusion	20 (11.2)	14 (7.9)	144 (80.9)
	MIC	2 (6.1)	1 (3.0)	30 (90.9)
	Multi/other	1 (2.3)	1 (2.3)	42 (95.5)
	Total	32 (6.3)	71 (14.0)	405 (79.7)

"Automated worst"

Caution – pip-taz interpretation in ESBL:s

Enterobacterales and piperacillin-tazobactam II

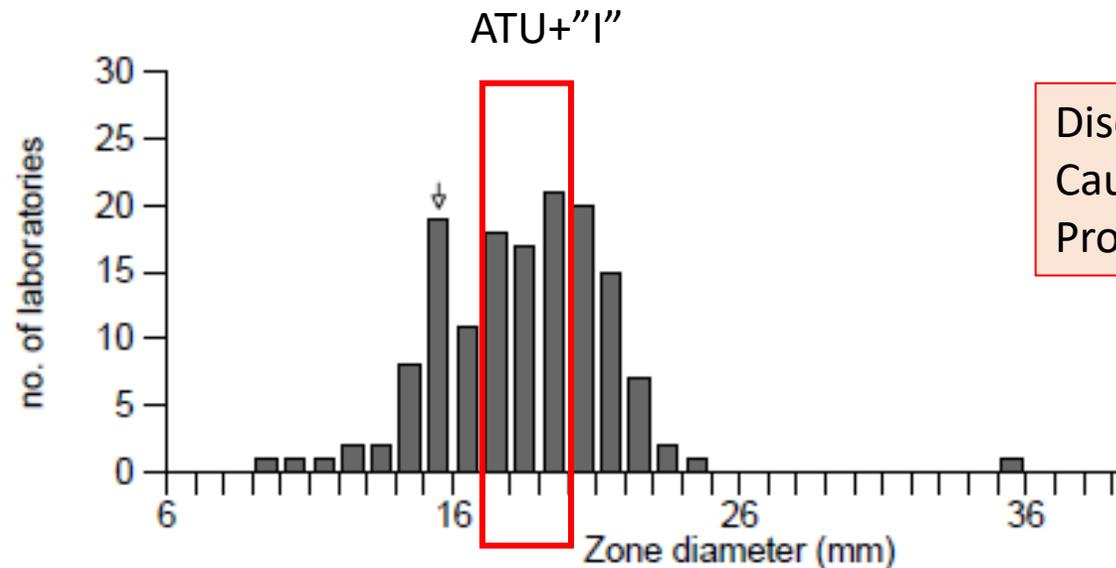
4527 *K.pneumoniae* ESBL-A (SHV5) Reference labs: PTZ MIC >64, >64 **Resistant**

Breakpoints: S ≤ 8 R > 16 mg/L S ≥ 20 R < 17 mm ATU 16mg/L ; 17-19mm

	Piperacillin-tazobactam			% concordance
	S	I	R	
SE	3	9	8	
NO	6	3	8	
DK	11	1	0	
FI	3	2	12	
EUCAST	107	48	340	70,5%

Table 2: Piperacillin-tazobactam susceptibility reports for *Klebsiella pneumoniae* specimen 4527.

Guideline	Method	n (%)* of participants reporting		
		S	I	R
EUCAST/EUCAST-related <small>DK 11 1 0</small>	Automated	29 (11.6)	1 (0.4)	220 (88.0)
	Disk diffusion	68 (40.5)	42 (25.0)	58 (34.5)
	MIC	6 (19.4)	0 (0.0)	25 (80.6)
	*Multi/other	4 (8.7)	5 (10.9)	37 (80.4)
	Total	107 (21.6)	48 (9.7)	340 (68.7)



Disc diffusion "worst",
Caution – pip-taz interpretation in ESBL:s
Problems despite ATU

Enterobacterales and carbapenems meropenem intermediate

4227 *K.pneumoniae* OXA-48 ESBL-CARBA CPE Reference labs: MER MIC 4, 4 **Intermediate**

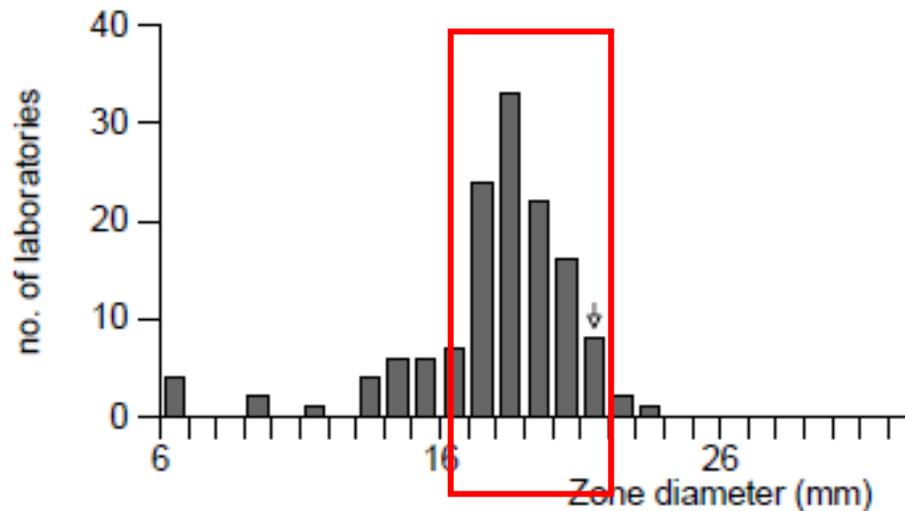
Breakpoints: S≤2 R>8 mg/L S≥22 R<16 mm Screen breakpoint <28mm/, > 0,125 ATU none

	Meropenem			% concordance
	S	I	R	
SE	4	15	4	
NO	3	12	2	
DK	1	7	4	
FI	6	6	6	
EUCAST	209	191	115	37,1%

Intermediate

Table 1: Meropenem susceptibility reports for *Klebsiella pneumoniae* specimen 4227.

Guideline	Method	n (%)* of participants reporting		
		S	I	R
EUCAST/EUCAST-related	Automated	34 (48.6)	23 (32.9)	13 (18.6)
	Disk diffusion	86 (31.9)	120 (44.4)	64 (23.7)
	MIC	50 (50.5)	20 (20.2)	29 (29.3)
	Multi/other	39 (51.3)	28 (36.8)	9 (11.8)
	Total	209 (40.6)	191 (37.1)	115 (22.3)



Low concordance for all methods.

Note that "MIC" do not solve the problem. Disc diffusion slightly better.

Clinical consequences

Enterobacterales and carbapenems II meropenem resistance

4431 *K.pneumoniae* IMP-1 ESBL-CARBA/ CPE Reference labs: MER MIC 16, 16 **Resistant**

Breakpoints: S≤2 R>8 mg/L S≥22 R<16 mm Screen breakpoint <28mm/, > 0,125 ATU none

	Meropenem			
	S	I	R	
SE	1	17	4	
NO	1	8	7	
DK	2	2	7	
FI	0	8	9	
EUCAST	55	117	336	66,1%

Intermediate

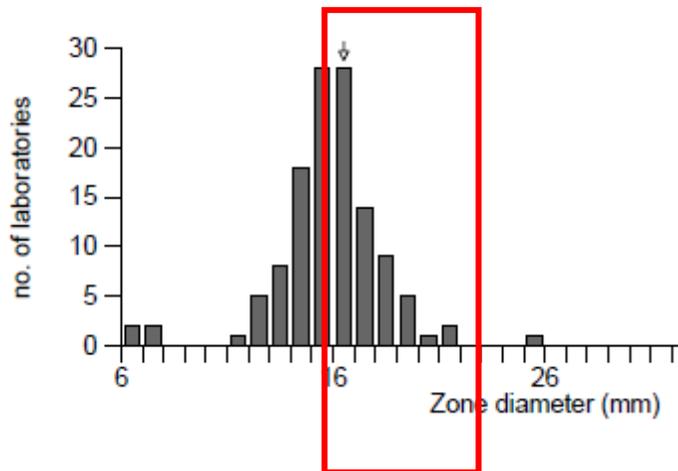


Table 4: Meropenem susceptibility reports for *Klebsiella pneumoniae* specimen 4431.

Guideline	Method	n (%)* of participants reporting		
		S	I	R
EUCAST/EUCAST-related	Automated	9 (4.6)	21 (10.8)	165 (84.6)
	Disk diffusion	21 (12.0)	63 (36.0)	91 (52.0)
	MIC	19 (24.4)	15 (19.2)	44 (56.4)
	Multi/other	6 (9.5)	18 (28.6)	39 (61.9)
	Total	55 (10.8)	117 (22.9)	339 (66.3)

In this isolate "Automated methods" give the best results
Clinical consequences

Enterobacteriales

Isolate	Species	Pattern/ Resistance	Mechanism/s
4347	E.coli	R. AMP, AMC	TEM-1
4179	E.coli	pAmpC/ ESBL-M R: ETP, PTZ	<i>bla</i> CMY-2 + porin loss
4391	E.coli	ESBL-A, R: AMI, GEN, TOB	TEM-1, ESBL CTX-M-15,OXA-1
4527	K.pneumoniae	ESBL-A, I: AMI, R: PTZ, AMC , GEN, TOB	<i>bla</i> SHV-5, aacA1, aacA4
4227	K.pneumoniae	CPE/ ESBL-CARBA I: MER, CTX	TEM-1, OXA-48
4431	K.pneumoniae	CPE/ESBL-CARBA, R: MER , CTX, GEN, TOB	TEM-1, IMP-1,OXA-2
4571	E.cloacae	CPE/ ESBL-CARBA, R: IMI , AMI, CIP, GEN, TIG, TOB	TEM-1, CTX-M-15,OXA-1, CMY NDM-1

- Good performance on detection of ESBL and Carbapenems
- Problems when levels of resistance (S/ I /R) in affected betalactams are reported

Non-fermenters

Isolate	Species	Pattern/ Resistance
4133	P.aeruginosa	OrpD+hyper-AmpC, R: AMI, CIP, GEN, IMI, MER, PTZ, TOB
4479	A. baumannii complex	S. MER R: GEN, CIP
4660	P.stutzeri	-
4346	S.maltophilia	-

- Good performance – no challenges
- Failure in Kalmar - Acinteobacter

Failure in Kalmar- Acinetobacter

4479 Acinetobacter baumannii complex versus meropenem

Sensitive

Breakpoints: S \leq 2 R $>$ 8 mg/L S \geq 21 R $<$ 15 mm

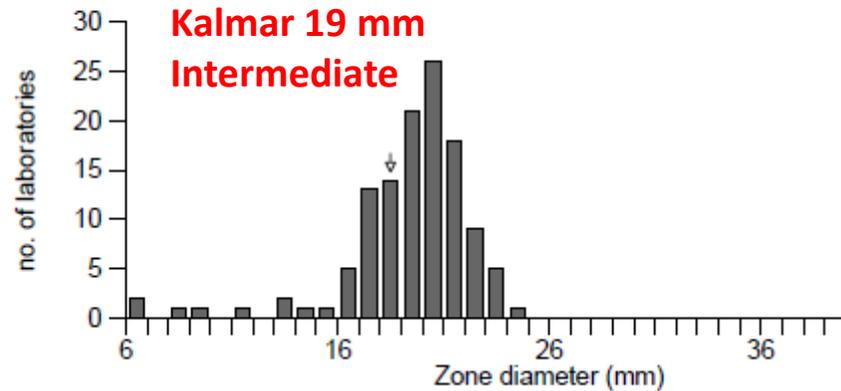
ATU: none

Meropenem - specimen 4479

Intended result : susceptible

Your guideline : EUCAST

■ EUCAST - Disk diffusion EUCAST



Why? Annoying! – should be sent to reference laboratory, when "Intermediate"

Failure in Kalmar- Acinetobacter

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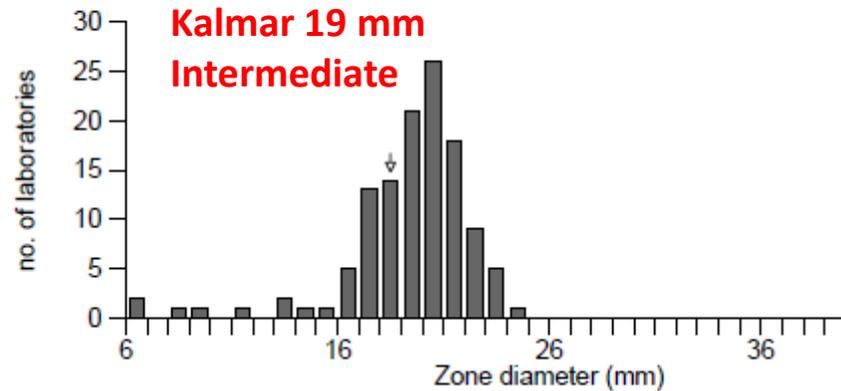
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Why? Annoying – should be sent to reference laboratory, when "I"

1) Retest of saved isolate: 20mm I, gradient test: 2 mg/L S

Failure in Kalmar- Acinetobacter

4479 Acinetobacter baumannii complex versus meropenem

Sensitive

Breakpoints: S≤2 R>8 mg/L S≥21 R<15 mm

ATU: none

Why? Annoying – should be sent to reference laboratory, when "I"

1) Retest of saved isolate: 20mm I, gradient test: 2 mg/L S

2) Internal control problems? – NO, within range

<i>P.aeruginosa</i> CCUG 17619									
Datum	Ptz 23-29	Cfz 21-27	Mer 27-33	Gen 17-23	Cip 25-33	Satt	Läst	Tillv dat	Ko
2019-04-26	27	25	32	20	28	SAP	KF	2019-04-12	
2019-04-29	26	24	31	19	30	KF	JF	2019-04-12	
2019-05-02	24	24	28	18	29	SAP	JF	2019-04-17	
2019-05-03	27	24	29	20	30	JF	JF	2019-04-12	
2019-05-06	27	24	30	19	31	JG	CK	2019-04-12	
2019-05-08	26	24	30	20	30		EL	2019-04-17	
2019-05-09	25	23	29	19	30	EL	AJ	2019-04-30	
2019-05-10	26	23	28	19	31	AJ	CAL	2019-04-30	
2019-05-13	27	24	30	20	31	ÅG	AK	2019-05-13	
2019-05-15	27	24	31	20	30	VH	KF	2019-04-30	
2019-05-16	26	25	30	19	30	KF	KF	2019-05-07	
2019-05-17	27	24	31	19	29	KF	KF	2019-05-07	
2019-05-20	27	25	32	20	31	CK	AK	2019-05-07	
2019-05-22	25	24	30	19	29	EL	EL	2019-05-10	

Failure in Kalmar- Acinetobacter

4479 *Acinetobacter baumannii* complex versus meropenem

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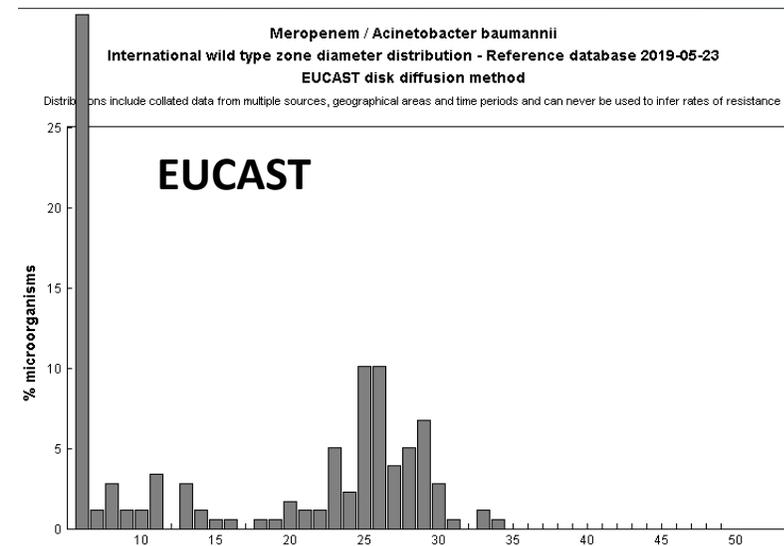
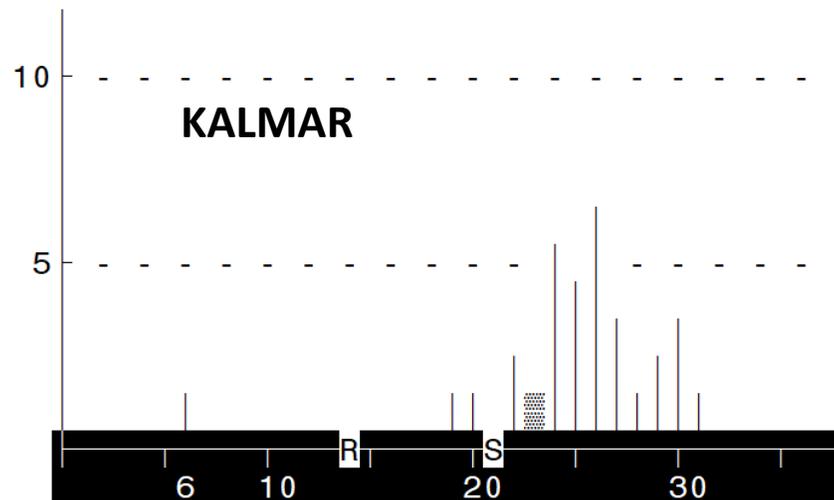
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Why? Annoying – should be sent to reference laboratory, when "I"

1) Retest of saved isolate: 20mm I, gradient test: 2 mg/L S

2) Internal control problems? – NO, within range

3) Clinical distribution problems? – NO, fits well to EUCAST



Failure in Kalmar- Acinetobacter

4479 *Acinetobacter baumannii* complex versus meropenem

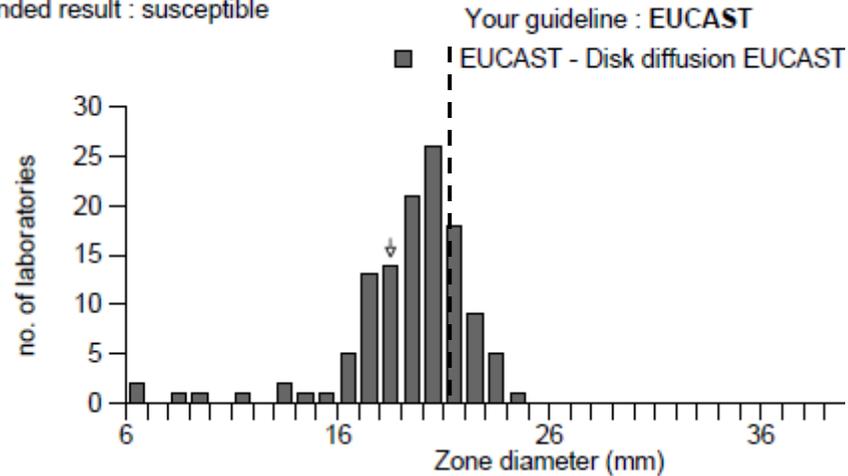
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ATU: none

Meropenem - specimen 4479

Intended result : susceptible

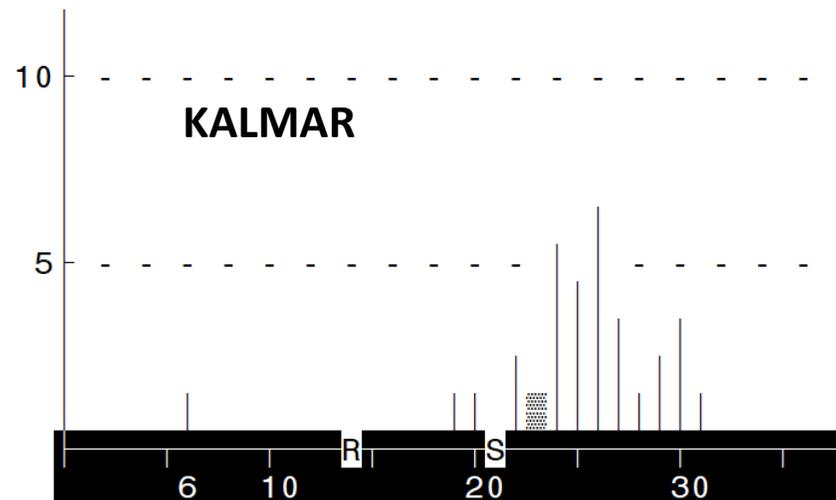


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UKNEQAS histogram - deviation from Kalmar clinical distribution



Failure in Kalmar- Acinetobacter

4479 Acinetobacter baumannii complex versus meropenem

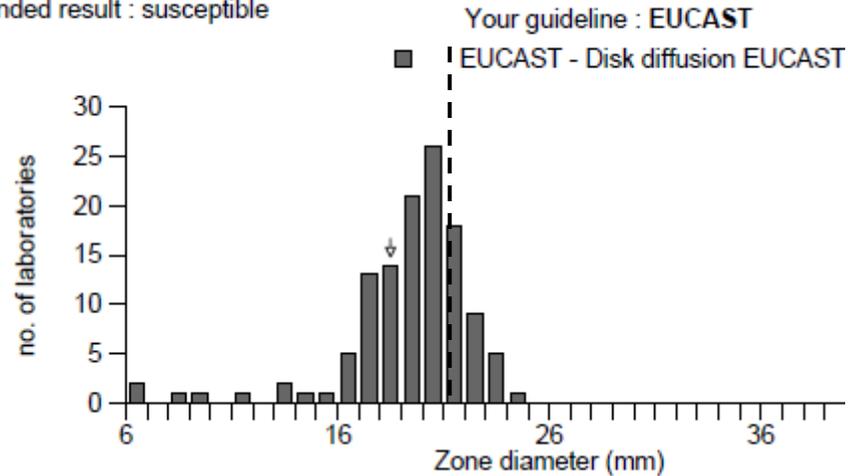
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 UKNEQAS histogram - deviation from Kalmar clinical distribution
 UKNEQAS results - we were not alone

Result by guideline

	S	I	R	% concordance
score	2	1	0	
BSAC	12	2	0	85.7
EUCAS	411	65	13	84.0
CLSI	74	3	2	93.7
NWGA	2	2	0	50.0
SRGA	1	1	0	50.0
All	500	73	15	85.0
SE	14	8	0	63.6

Failure in Kalmar- Acinetobacter

4479 Acinetobacter baumannii complex versus meropenem

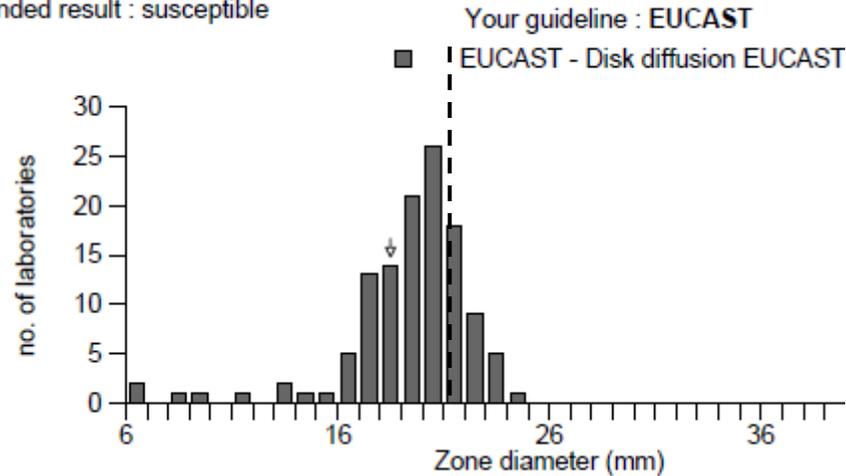
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Meropenem - specimen 4479

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SE	14	8	0	63.6

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1) Retest of saved isolate: 20mm I, gradient test: 2 mg/L S

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3) Clinical distribution problems? – NO, fits well to EUCAST
UKNEQAS histogram indicate non-native organism
UKNEQAS results show- we were not alone

4) Conclusion: Not a wild type isolate even if categorized as sensitive – judged as minor error in Kalmar

Failure in Kalmar- Acinetobacter

4479 *Acinetobacter baumannii* complex versus meropenem

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ATU: none

Why? Annoying – should be sent to reference laboratory, when "I"

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UKNEQAS histogram indicate non-native organism

UKNEQAS results show- we were not alone

4) Conclusion: Not a wild type isolate even if categorized as sensitive – judged as minor error in Kalmar

5) One year later:

"Whole genome sequencing showed the presence of the *bla*OXA-66 gene, a variant of the chromosomal *bla*OXA-51 found in *Acinetobacter baumannii*, and encoding the OXA-66 betalactamase.

This enzyme has carbapenemase activity, although phenotypic resistance in isolates depends on the level of expression of the enzyme and other factors such as efflux or reduced permeability."

Others

Isolate	Species	Pattern/ Resistance
4659	B.fragilis	R: MZL, PTZ
4226	H.influenzae	Betalactamase positive
4611	M.catarrhalis	-
4705	C.jejuni	R: CIP

- Some underestimating resistance to metronidazole and piperacillin-tazobactam in Bacteroides

Summary

- Overall: Relevant challenges and good performance
- Problems with distinguishing different levels of acquired resistance towards betalactams

Wishes to UKNEQAS:

- Better specification of methods used: What is "MIC"?
- Challenges on H.influenzae, S.aureus- vankomycin, VRE vanB and more
- Reports on resistance genes somewhat earlier...?
- Fuse report on "EUCAST related" (NWGA, SRGA, BSAC)