Standardised methods and harmonised guidelines for antimicrobial susceptibility testing - an international external quality assessment provider's perspective

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Introduction

Participants of the United Kingdom National External Quality Assessment Service (UK NEQAS) international scheme for antimicrobial susceptibility testing (AST) report susceptibility results interpreted primarily according to either EUCAST or CLSI guidelines. The drive to standardise AST methods and harmonise guidelines is making good progress but EQA highlights some outstanding issues.

Guidelines and methods used by UK NEQAS participants

Guidelines followed by UK NEQAS participants (n = circa 670)

Guidelines	% Percent following guidelines	
	2010	2011
EUCAST	8.5	30.6
EUCAST-related	30.1	24.9
All EUCAST	38.6	55.5
CLSI	56.3	39.3
Other/combined	5.1	5.2

Methods used by UK NEQAS participants (n = circa 670)

Guidelines	% Percent using method		
	Automated	Disc	Other/ combined
EUCAST	53.0	37.7	9.3
EUCAST-related	8.3	78.3	13.4
CLSI	64.3	22.5	13.2
Combined/other	59.5	27.0	13.5

Methods

Performance of participants was analysed according to methods and guidelines used for recently distributed EQA specimens.

Definitions

EUCAST - European Committee on Antimicrobial Susceptibility Testing
CLSI – Clinical and Laboratory Standards Institute
SRGA – Swedish Reference Group for Antibiotics

Performance may be affected by breakpoint guidelines used

S. aureus 7240, ciprofloxacin MIC 0.5 mg/L

Guidelines	Breakpoints (mg/L)		Number of laboratories reporting		
	S≤	R>	S	I	R
CLSI	1	2	334	5	4
BSAC	1	1	167	19	1
SRGA	0.06	2	3	19	0

S. aureus 7876, ciprofloxacin MIC 0.25 mg/L

Guidelines	Breakpoints (mg/L)		Number of laboratories reporting		
	S≤	R>	S	I	R
CLSI	1	2	350	0	0
BSAC	1	1	176	0	1
SRGA*	1	1	23	2	1

- SRGA increased the susceptible breakpoint from 0.06 to 1mg/L following the EUCAST harmonization of breakpoints, resulting in increased concordance with the intended result for *S. aureus* 7876 in laboratories following these guidelines

Guidelines are not always followed

***S. aureus* specimen 9889 fusidic acid (MIC 4-8 mg/L)**

Guidelines	Breakpoints (mg/L)		% Percent of laboratories reporting		
	S≤	R>	S	I	R
CLSI	1	1	0	2.1	97.9
BSAC	-	-	1.0	40.1	58.9

- There are no CLSI breakpoints for fusidic acid

Performance is affected by method used

***E. faecalis* specimen 0138 vancomycin (MIC 8-16 mg/L)**

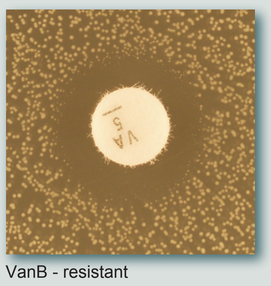
VanB EUCAST resistant, CLSI intermediate

Method	% Percent using method		
	S	I	R
Automated (n=333)	3.9	6.2	89.9
MIC (n=71)	2.8	13.9	83.3
Disk diffusion (n=262)	15.5	11.6	72.9

- Vancomycin MICs can be low for VanB strains, as in this case (MIC 8-16 mg/L), and the isolate would be interpreted as resistant by EUCAST breakpoints but intermediate by CLSI breakpoints. The borderline susceptibility makes detection of reduced susceptibility more difficult, particularly with disc diffusion methods, where the difference in zone diameter between susceptible and resistant isolates may be small and the appearance of a "fuzzy" zone edge or colonies just within the zone edge may be the best indication of resistance.

Detection of VanB glycopeptide resistance in enterococci by disc diffusion

Vancomycin susceptible



VanB - resistant

- Look for "fuzzy" zone edges or small colonies within zone edge

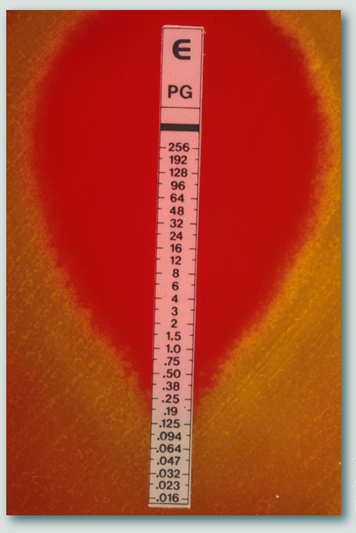
Borderline susceptibility reduces the reliability of results

Organism	Agent	Expected result	% reporting		
			S	I	R
E. faecalis 0138	Vancomycin	I/R	7.3	18.4	74.3
P. aeruginosa 0489	Pip-tazo	S/R	29.9	1.5	68.6
E. coli 0270	Pip-tazo	S/I	32.7	23.6	43.6
K. pneumoniae 0138	Cefuroxime	S	79.6	4.5	16.9
E. coli 0270	Amikacin	S	61.8	31.6	6.6
M. morganii 0447	Imipenem	S/I	78.3	12.6	9.1

- Variable reporting of susceptible, intermediate and resistant was increased for organism/agent combinations listed in the table above where susceptibility was borderline

Uncertainty in reporting penicillin susceptibility in *S. pneumoniae*

- Screen with oxacillin disc
- If resistant, MIC to define susceptibility



"Intermediate" to penicillin
Susceptible if from pneumonia
Resistant if from meningitis

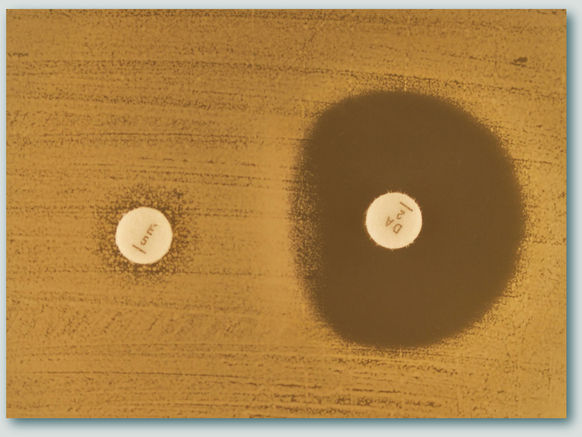
***S. pneumoniae* specimen 0272 (EARS-Net) penicillin MIC 0.5 mg/L**

Laboratories reporting	Interpretation		% Percent reporting		
	EUCAST	CLSI	S	I	R
Oxacillin (n=523)	R	R	4.6	4.6	90.8
Penicillin:					
Pneumonia (n=740)	S	S	76.1	20.8	3.1
Meningitis (n=741)	R	R	5.5	8.1	86.4

- The participants' results for penicillin without a site of infection cannot be interpreted as guideline breakpoints relate to the site of infection. Significant numbers of participants interpreted the isolate as intermediate in susceptibility to penicillin irrespective of whether the isolate was from meningitis (8.1% reported intermediate) or from pneumonia (20.8% reported intermediate). These differences will partly relate to national differences in reporting practices.

Uncertainty in reporting dissociated resistance to clindamycin in *S. aureus*

***S. aureus* with dissociated (MLSB-inducible) resistance to clindamycin**



***S. aureus* specimen 0275 (EARS-Net)**
Clindamycin (MIC 0.12-0.5 mg/L, but resistance induced by erythromycin)

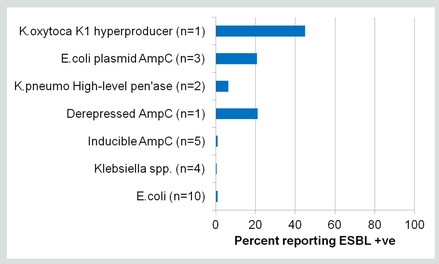
Percent laboratories reporting (n=775)		
S	I	R
24.0	1.8	74.2

Reports of susceptible not related to guideline or method

- EUCAST expert rules recommend reporting resistant, or susceptible with warning of possible failure due to selection of resistant mutants. Avoid use in serious infections
- CLSI – report resistant with note that some may respond

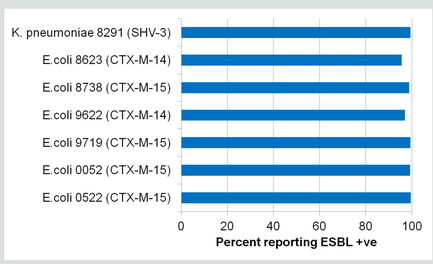
Detection of ESBL-mediated resistance in Enterobacteriaceae

Detection of ESBLs in Enterobacteriaceae



- ESBL reporting in Enterobacteriaceae without ESBLs was more variable

Reports of ESBLs in Enterobacteriaceae without ESBLs



- More than 97% of participants reported ESBL +ve for the Enterobacteriaceae with ESBLs listed in the table above

Conclusion

- Performance can be linked to guidelines and methods used for some tests
- Discrepancies more common when:
  - Critical differences between guidelines
  - Failure to follow guidelines
  - Susceptibility borderline
  - Confusion over reporting

Summary

EQA is a valuable tool in the quality assurance of AST in the diagnostic laboratory. Discrepancies were identified mainly where there were differences in interpretation of breakpoints between guidelines and where adherence to the stated guideline was not observed.

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