

EUCAST News!

Species and agents supported (or not) by EUCAST breakpoints and methodology

Gunnar Kahlmeter

EUCAST Chairman 2001 – 2012,
EUCAST Clinical Data coordinator 2012 –
Sweden

NEQAS userday, 2015



Disclosures

- Consulting for Oxoid, Thermofisher, on technical issues
- The EUCAST Development laboratory constantly work with pharmaceutical companies and AST manufacturers to develop good quality AST products.

EUCAST 2015

- Rafael Canton, ES (Chair)
- Derek Brown, UK (Scientific secretary)
- Gunnar Kahlmeter, S (Webmaster)
- Alasdair MacGowan/Robin Howe, BSAC
- Gerard Lina, CA-SFM
- Johan Mouton, CRG
- Christoffer Lindemann, NWGA
- Christian Giske, SRGA
- Sören Gatermann, German NAC
- Jan Verhaegen, GC (Belgium)
- Iztok Strumbelj, GC (Slovenia)

Structure

- EUCAST is a European Committee set down by ESCMID and with formal ties to ECDC, EMA and EFSA.
- Network of National AST Committees (NACs).
- Financed by ESCMID and ECDC.
- Five 2-day meetings per year.
- Public consultation process.
- Laboratory network (bacteria and fungi).

How is EUCAST doing?

Implementation of EUCAST breakpoints, Late 2015

% Laboratories

- >50%
- 10-50%
- <10%
- No information

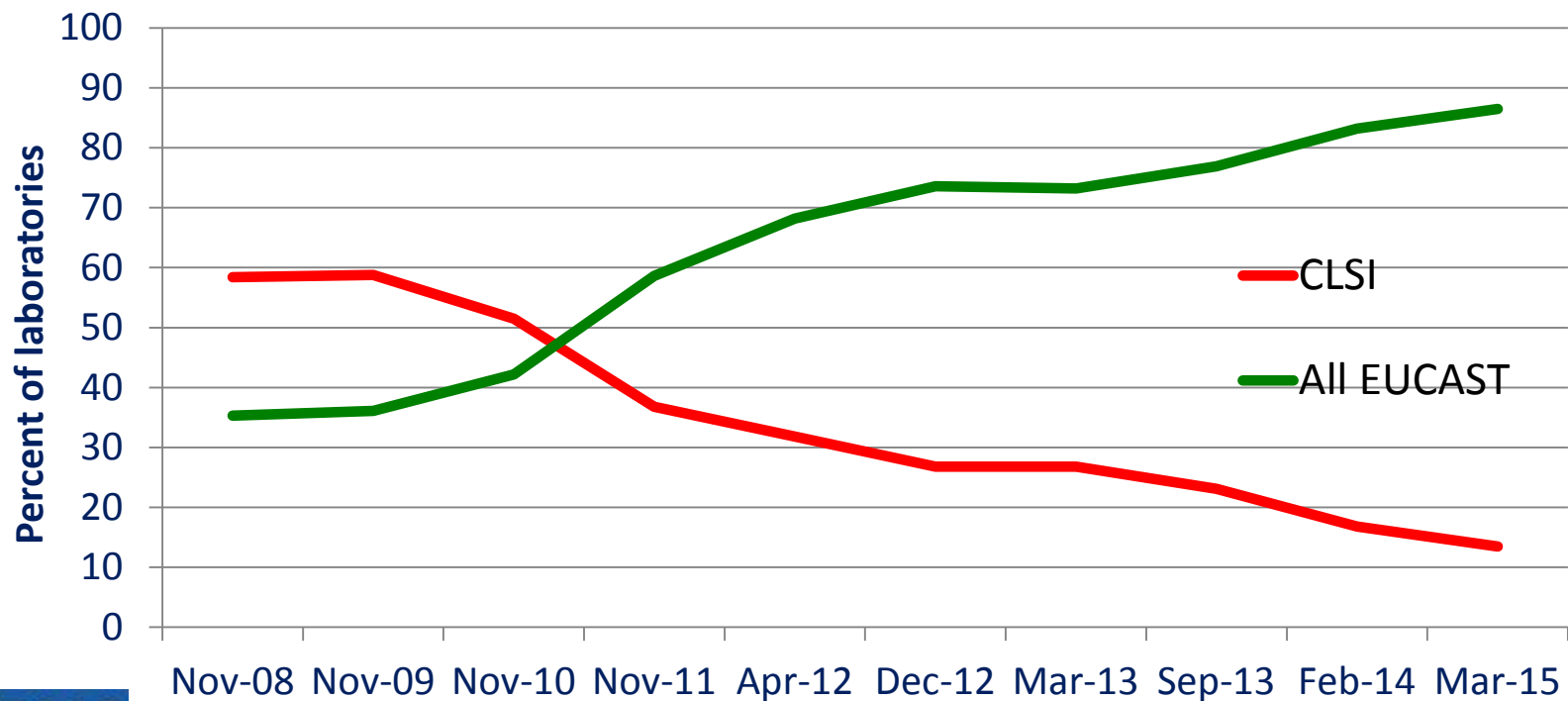


Countries not on this map: Australia Brazil Iceland Israel Morocco New Zealand South Africa

Widespread implementation of EUCAST breakpoints for antibacterial susceptibility testing in Europe

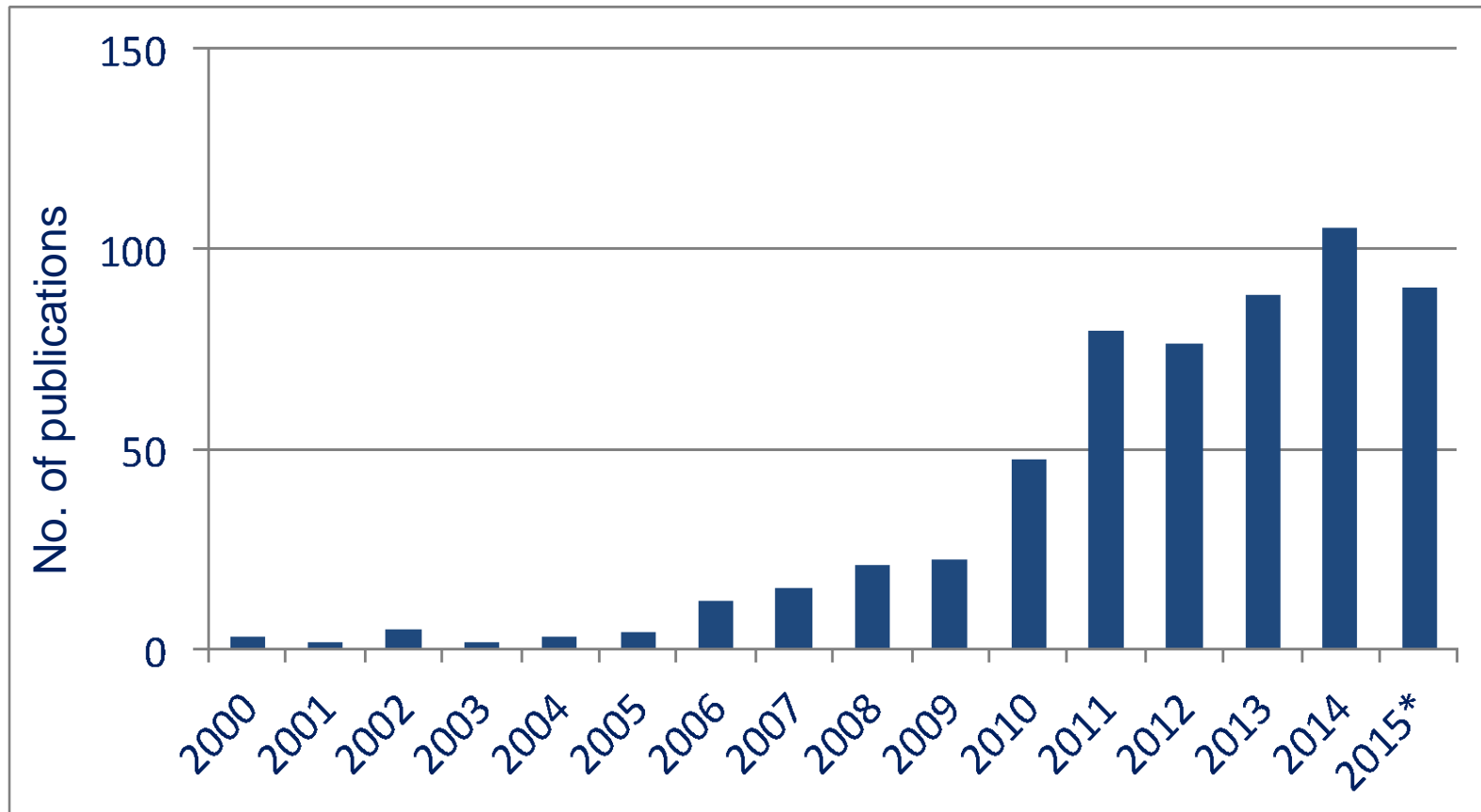
D Brown¹, R Cantón (rafael.canton@salud.madrid.org)², L Dubreuil³, S Gatermann⁴, C Giske⁵, A MacGowan⁶, L Martínez-Martínez⁷, J Mouton⁸, R Skov⁹, M Steinbakk¹⁰, C Walton¹¹, O Heuer¹², M J Struelens¹², L Diaz Högberg¹², G Kahlmeter¹³

Uptake of EUCAST guidelines by participants in UKNEQAS (*updated*) (630-750 participants per year from a total of 40 countries)



EUCAST-related publications

- Publications (PubMed) including “EUCAST” in the title or abstract



*Jan 1 - Sept 15, 2015

EUCAST 2002 - 2015

2002

- BSAC (UK)
- CA-SFM (F)
- CRG (NL)
- DIN (D)
- NWGA (N)
- SRGA (S)

- CLSI



2015

- EUCAST

- CLSI

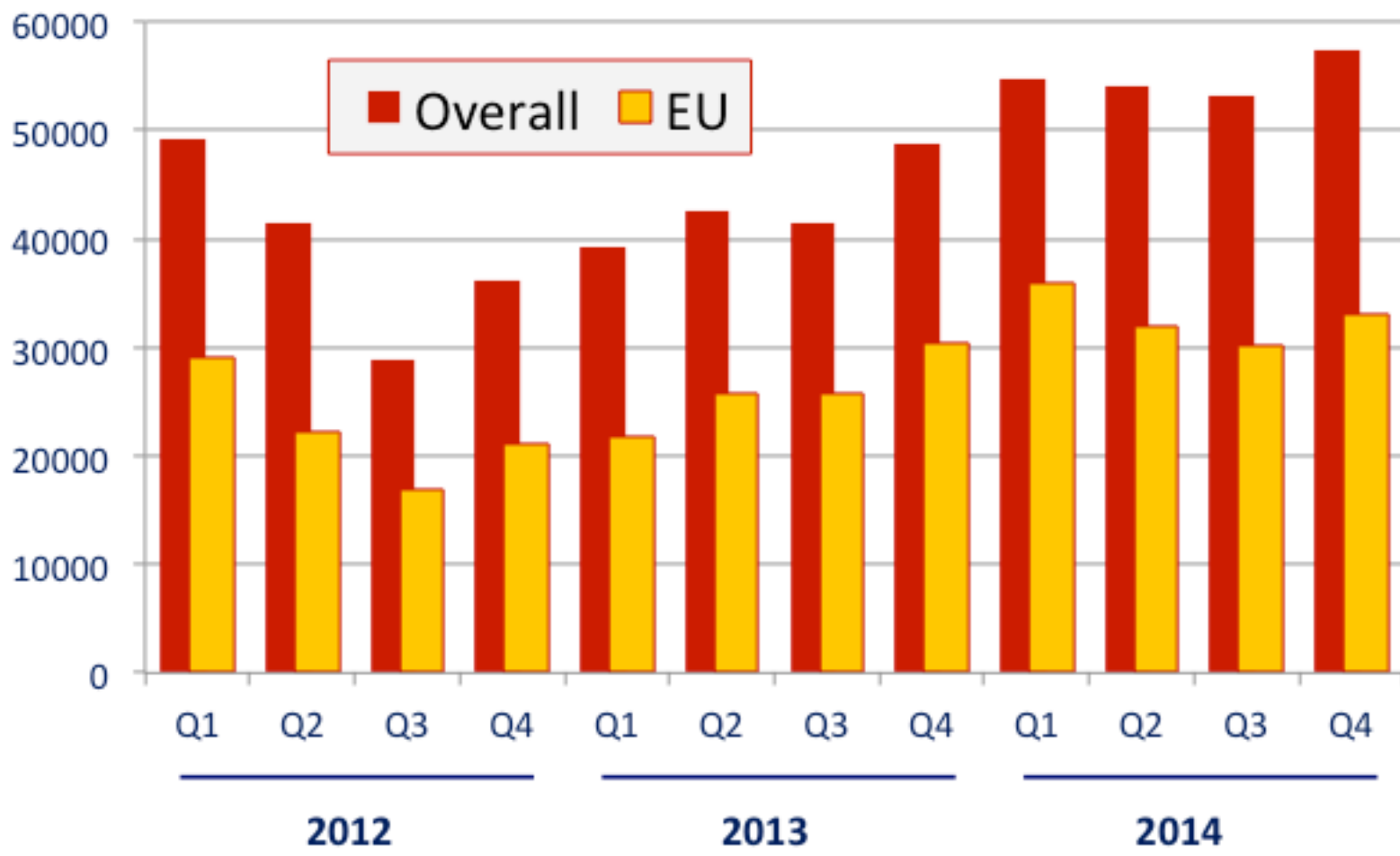
EUCAST Website visits

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- Guidance doct
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- Zone distributi
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- AST of fungi
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Disk diffusion tests

In the “old days”

- (DIN) - Germany

2015

- EUCAST

[J Antimicrob Chemother.](#) 2015 Sep 16. pii: dkv287. [Epub ahead of print]

Antimicrobial susceptibility testing breakpoints and methods from BSAC to EUCAST.

[Brown DF](#)¹, [Wootton M](#)², [Howe RA](#)².

Abstract

.... and BSAC will replace support of its own disc diffusion method with support for the EUCAST method from January 2016.

- CLSI - USA

EUCAST News

- Breakpoint table v. 6.0 (1 Jan, 2016)
- International representation on SC increased
- New subcommittees formed
 - Mycobacteria
 - The role of whole genome sequencing in AST
 - Veterinary AST
 - MIC distributions and ECOFFs
- New breakpoints
 - Ceftobiprole, Lipoglycopeptides (orita-, dalba- and telavancin), Tedizolid

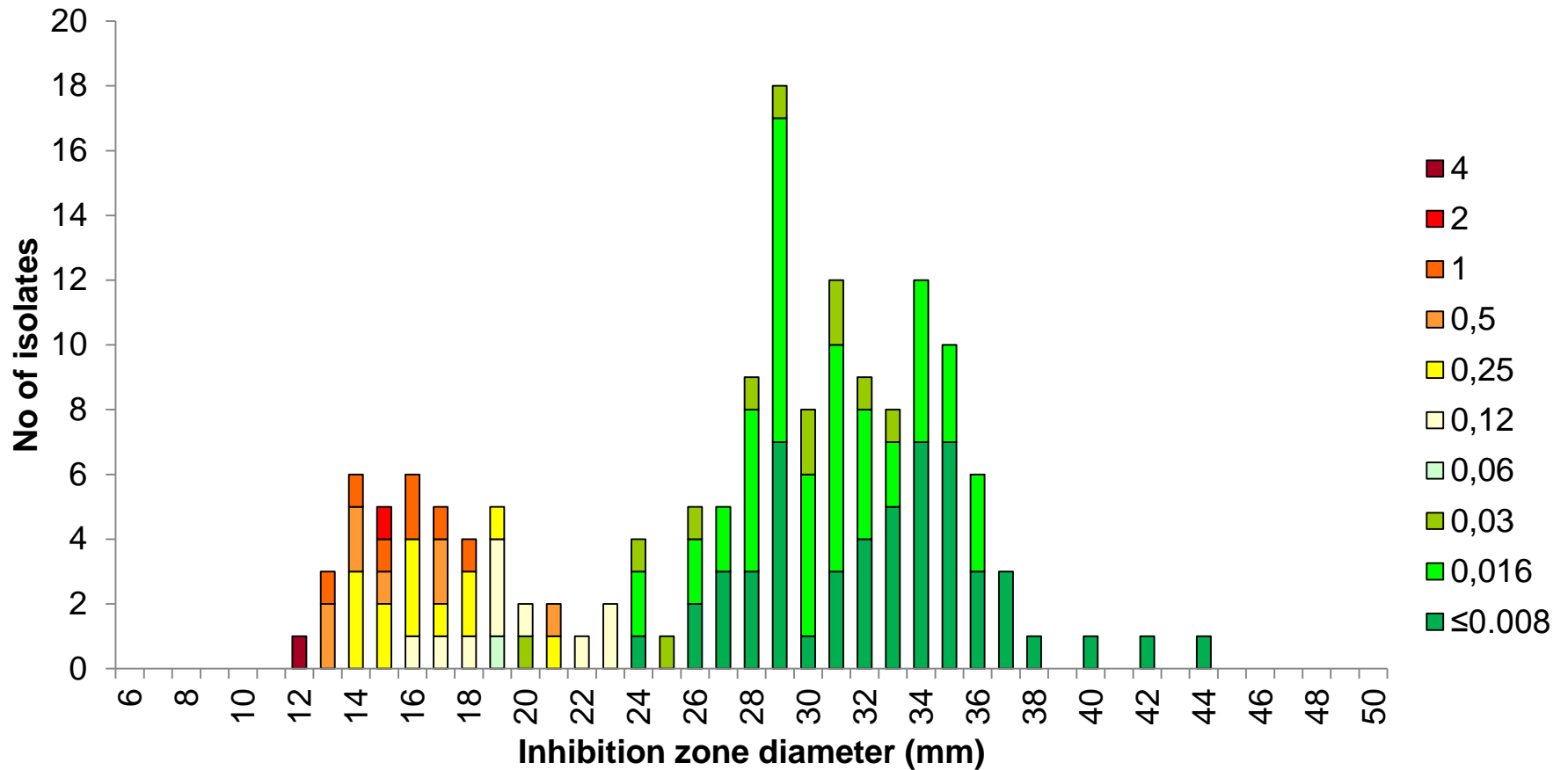
EUCAST News

- Review of breakpoints
 - Fluoroquinolones, Carbapenems, Colistin, Macrolides, Aminoglycosides
- Guidance notes in preparation
 - Daptomycin and Enterococcus spp (no breakpoints, only guidance)
 - What to do when there are no breakpoints?
- Breakpoint table for rapid (8h) disk diffusion AST
- New contract with ECDC (3 years)

Bacteria where breakpoints and methods are being developed

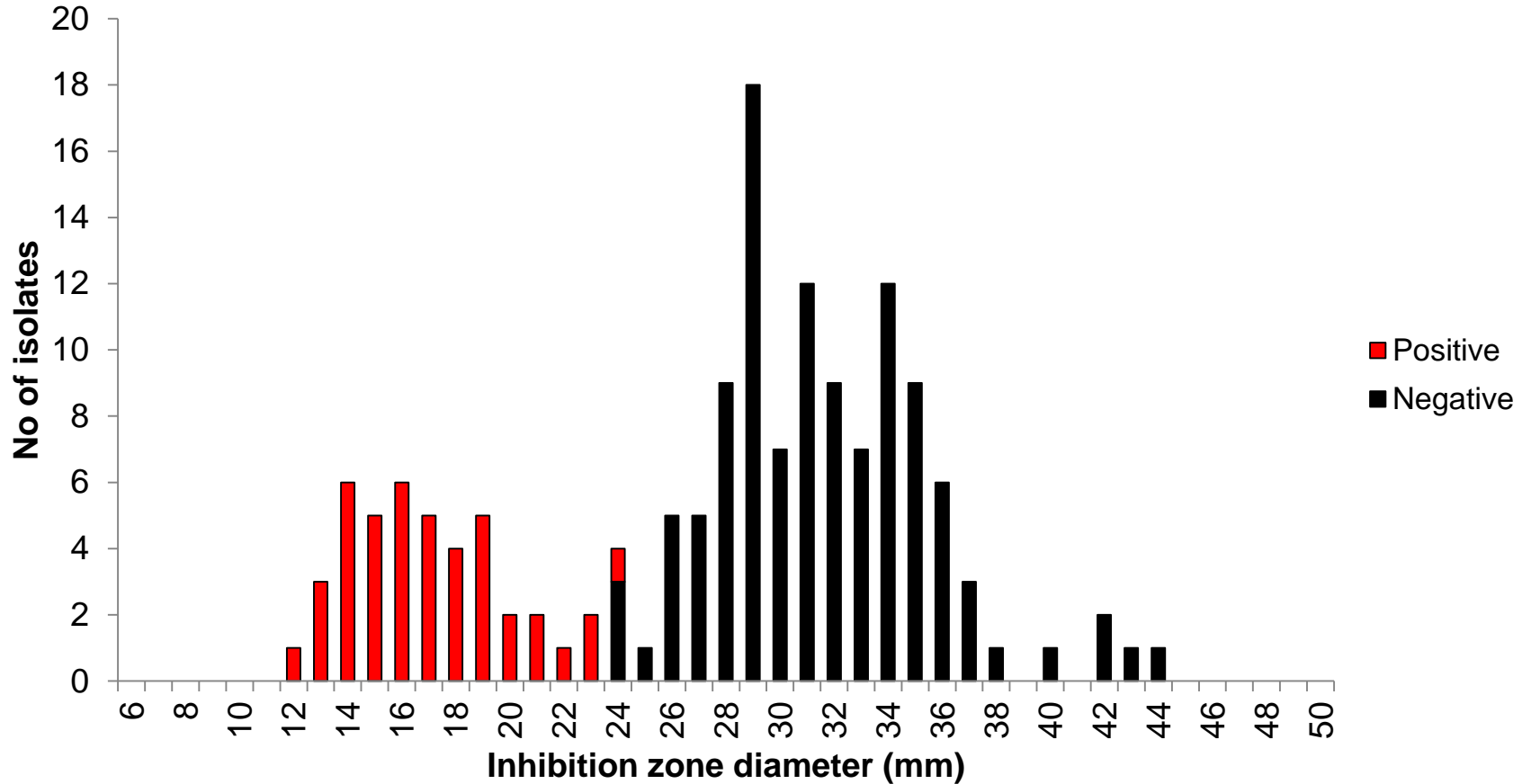
Aerococcus spp.	Bpts + methods	2016
Kingella kingae	Bpts + methods	2016
Aeromonas spp.	Bpts + methods	2016
Actinomyces, Nocardiae	Bpts + methods	2017-18
N. meningitidis	MIC-testing	
N. gonorrhoeae	MIC-testing	Disk test ?
Anaerobes	MIC-testing	Disk test ?
...		

Benzylpenicillin 1 unit vs. MIC *Kingella kingae*, 156 clinical isolates

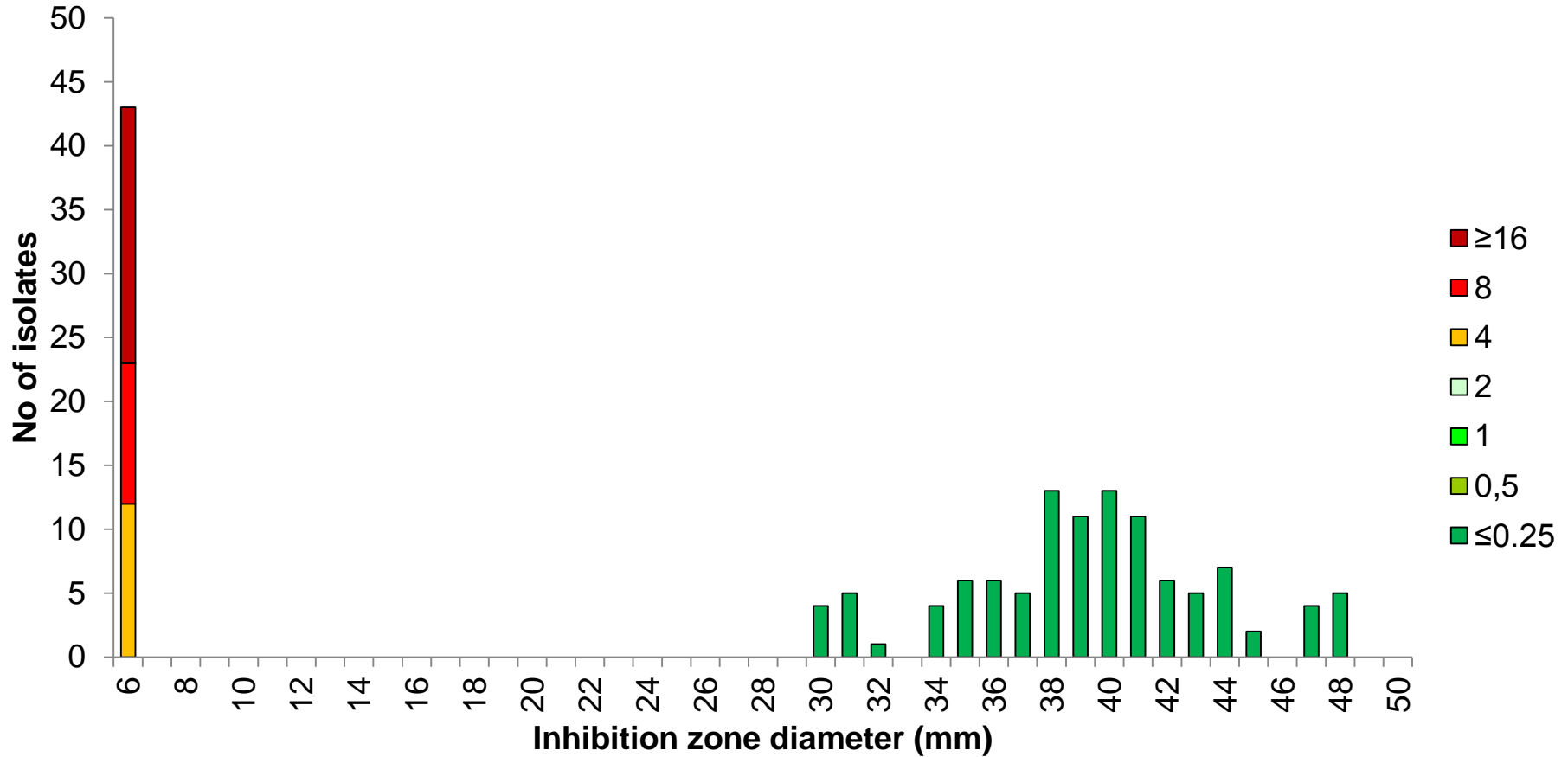


Cooperation between EUCAST and Pablo Yagupsky, Israel

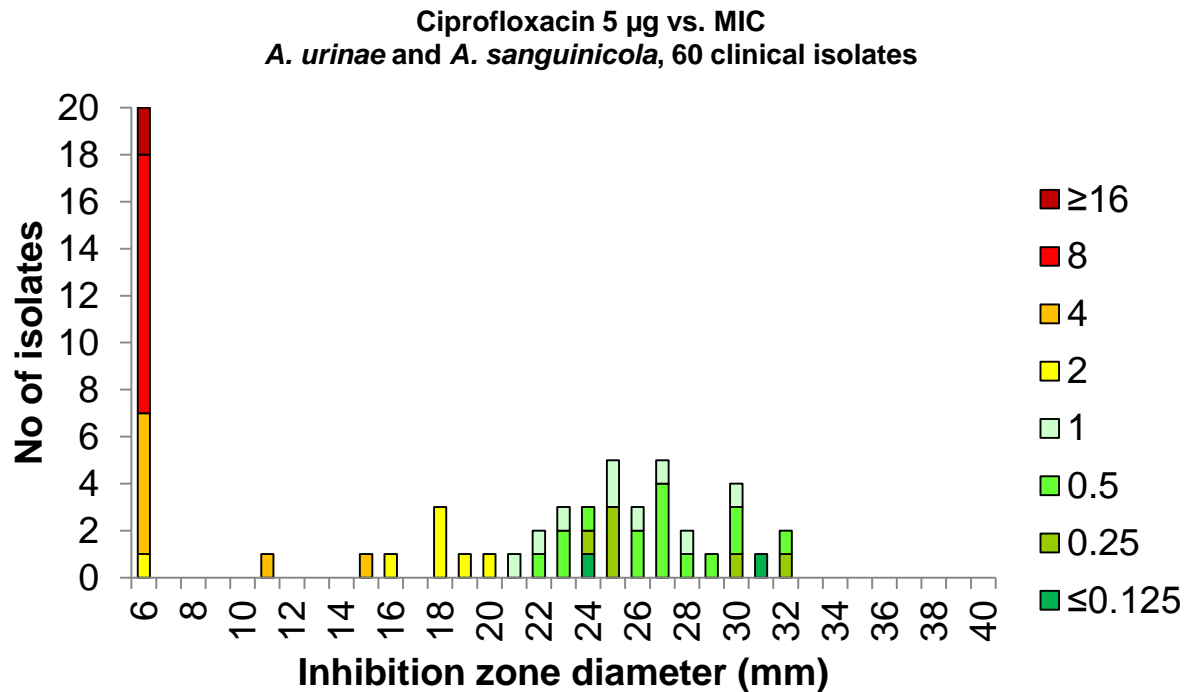
Benzylpenicillin 1 unit vs. beta-lactamase *Kingella kingae*, 155 clinical isolates



Trimethoprim-sulfamethoxazole 25 µg vs. MIC *Kingella kingae*, 151 clinical isolates

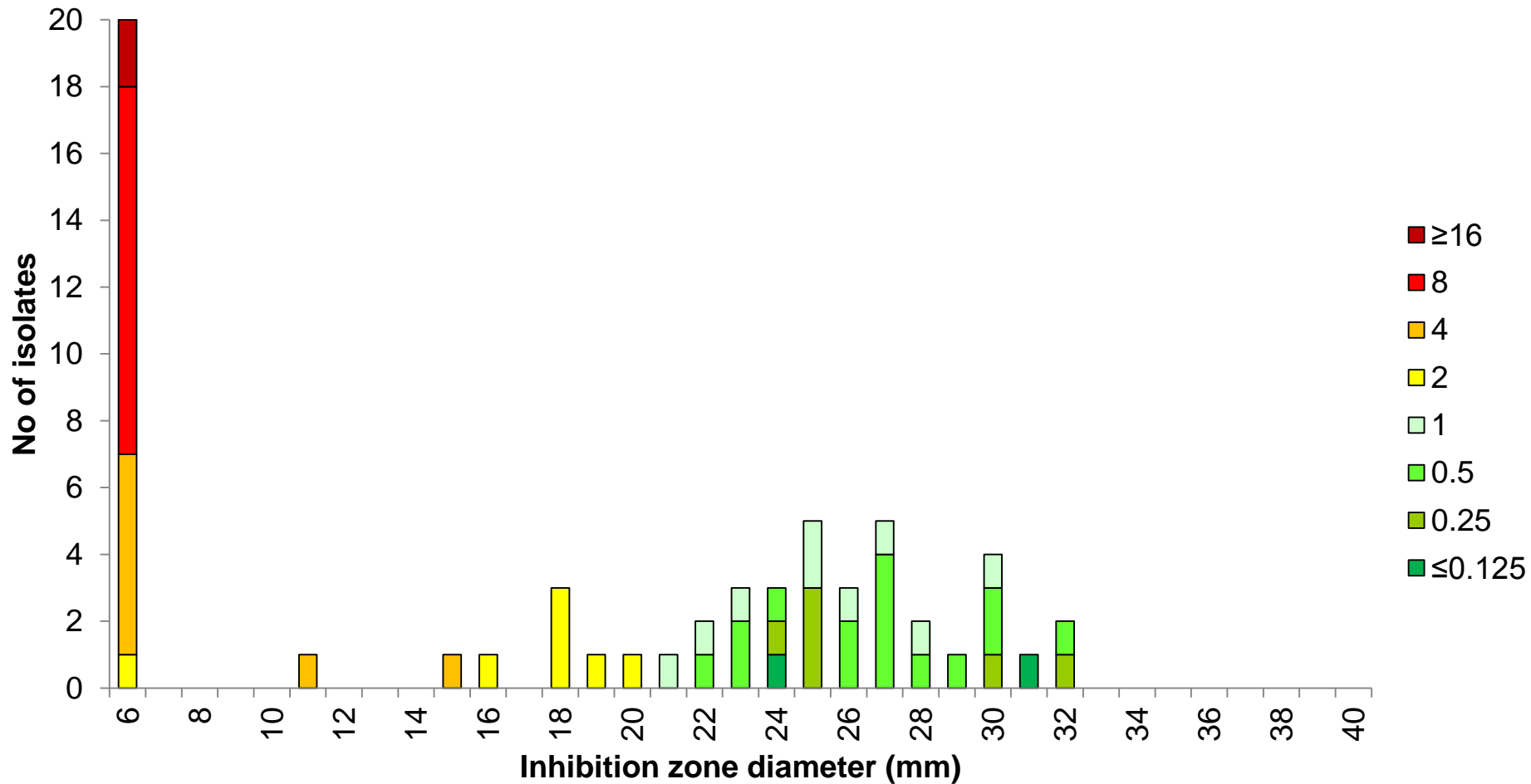


Aerococcus urinae and *A. sanguinicola* MIC-zone diameter correlates



Ciprofloxacin 5 μ g vs. MIC

A. urinae and *A. sanguinicola*, 60 clinical isolates



Fosfomycin disk diffusion in 2016

...or not at all!

Enterobacteriaceae (and *P. aeruginosa*)
MIC-zone diameter correlates for
ceftolozane-tazobactam

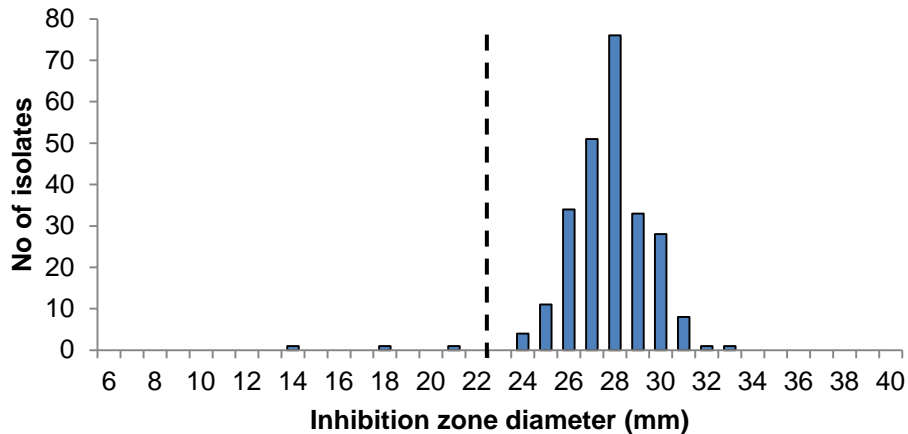
EUCAST Development Laboratory (EDL)

Update December 2015

Figure 2. Inhibition zone diameter distribution for consecutive *E. coli* from 5 additional laboratories

a) Ceftolozane-tazobactam 30-10 µg

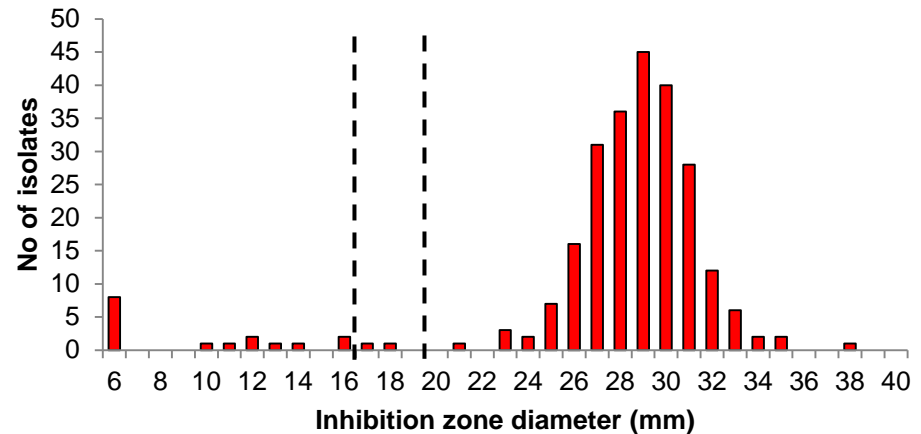
**Ceftolozane-tazobactam 30-10 µg
E. coli, 50 isolates x 5 sites (n=250)**



Mast disks (3 laboratories)
Bio-Rad disks (2 laboratories)
MH from 4 manufacturers

b) Cefotaxime 5 µg (control agent)

**Cefotaxime 5 µg (Oxoid disks)
E. coli, 50 isolates x 5 sites (n=250)**



***E. coli* and cefotaxime 5 µg**
EUCAST ECOFF: 23 mm
Median ± 1 mm from reference distribution

EUCAST rapid phenotypic AST

- Validation of short-incubation (6 – 8 h) of EUCAST standard disk diffusion methodology.
- Validated against the full 16-20h incubation with an inoculum based on inoculating positive blood culture medium 1/10 directly to MH plates.
- To be used primarily for rapid AST in bloodstream infections. Blood culture bottles positive in the morning can be AST:d for 16.00. Bottles positive in the evening can be AST:d for next early morning.
- Limited number of pathogens and limited number of antimicrobial agents.

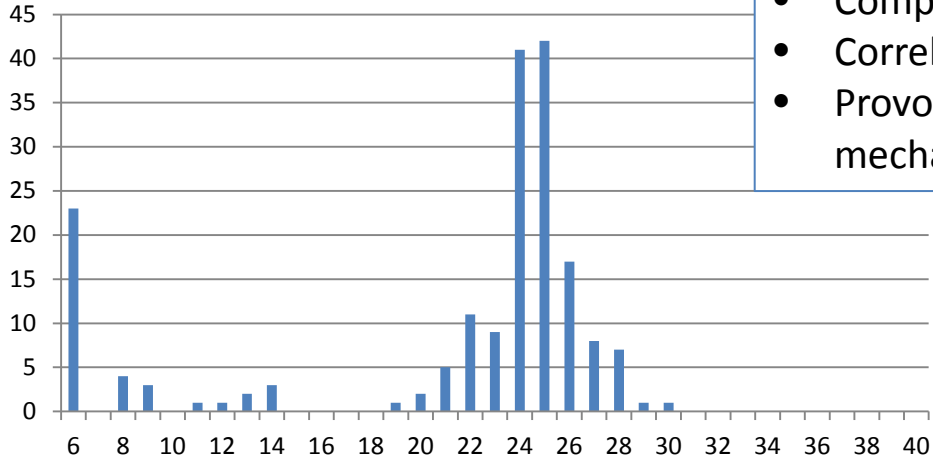
Analysis of results from rapid AST

E. coli with cefotaxime 5 µg

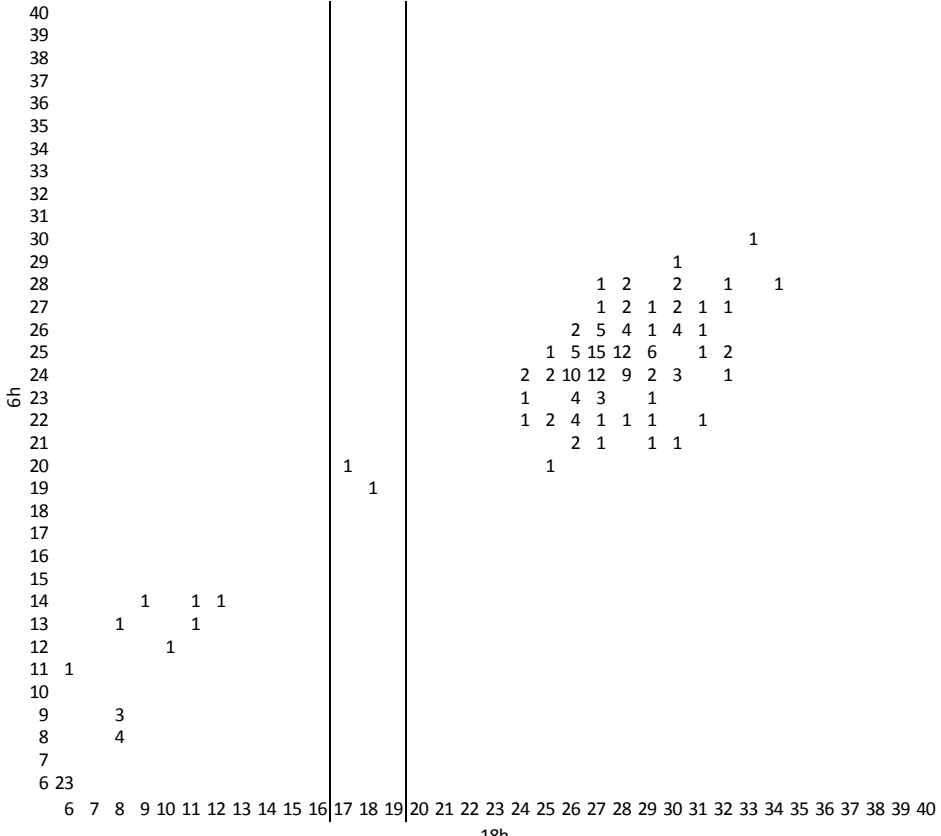
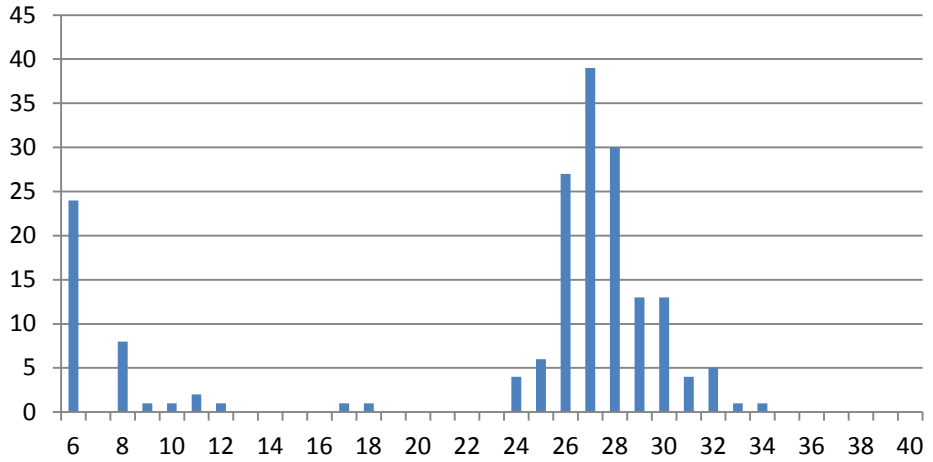
6 h

On-going work:

- Comparison of distributions (median, ECOFF) (6 h vs. 18 h)
- Correlation with standardised DD
- Provoking the system with isolates with known resistance mechanisms.



18 h



Colistin – subcommittee interim report (I)

- MIC testing – no change in methodology
- Disk diffusion still not possible
- MIC distributions on www.eucast.org mostly valid but more data needed

- Breakpoints and methods needed for
 - Enterobacteriaceae
 - Pseudomonas
 - Acinetobacter

Colistin – subcommittee interim report (II)

Current EUCAST breakpoints are

- Enterobacteriaceae $S \leq 2 / R > 2$ mg/L
- Acinetobacter $S \leq 2 / R > 2$ mg/L
- Pseudomonas $S \leq 4 / R > 4$ mg/L

New breakpoints (under discussion between CLSI and EUCAST)

- Enterobacteriaceae 2 / 2 mg/L ECOFFs 2 mg/L
- Acinetobacter 2 / 2 mg/L ECOFF 2 mg/L
- Pseudomonas 2 / 2 (or 4 / 4) mg/L ECOFF 4 mg/L





- These breakpoints were selected on the basis of maximum dosing of colistin, and there is no room for an intermediate category.

- Since the breakpoints are equal to the ECOFFs, isolates categorised as resistant will harbor resistance mechanisms.

Disk quality – comparing disks from 9 manufacturers

Summary

- Large variation in disk content between manufacturers
- In a few cases (spot checks so far) also poor reproducibility within a batch
- New disk lots from some manufacturers were improved in second test
- The data now (22 Oct) available on EUCAST website.
Will companies use the results for marketing?

	Mean value within ± 1 mm of the target value
	Mean value >1 mm but within ± 2 mm of the target value
	Mean value >2 mm from target value but still within the QC range
	Mean value out of the QC range

NA = Not Available

H = High, mean value > 1 mm above target

L = Low, mean value > 1 mm below target

* Individual zones (≥ 1) out of QC range

EUCAST recommendations

(this slide not translated)

Green disks are close to the QC targets and well calibrated for use with the EUCAST disk diffusion method.

Yellow disks deviate from the QC targets, but the results are still acceptable. Manufacturers are advised to take note and review their manufacturing process.

Orange disks deviate significantly from QC targets. Laboratories are warned against the use of these disks and manufacturers are urged to immediately review their manufacturing process.

Red disks are completely out of range and most probably contain either less than half or more than twice of the nominal amount of the active agent. Laboratories are warned against the use these disks and manufacturers should withdraw them from the market.

Disks from nine manufacturers

Table 1. Evaluation of disks from nine manufacturers vs. EUCAST QC targets and ranges. 1 = First Study, 2 = Follow-up Study

Antimicrobial disk	Bio-Rad		Liofilchem		BD		Abtek		SirScan		Oxoid		HiMedia		Bioanalyse		Mast	
	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Benzylpenicillin 1 unit					L				H	H			NA	NA	H	H		
Amoxicillin-clav. 30 µg	H	H*					L						H	H		L		
Piperacillin-tazo. 36 µg							L	L	H				NA	NA				
Oxacillin 1 µg			L		L				L				H	H	L			
Mecillinam 10 µg							L		H				H		H			
Cefotaxime 5 µg							NA		L				NA	NA				
Cefoxitin 30 µg	H*	H*	H	H*			NA	L					L*	L*		L		
Ceftazidime 10 µg							L	L					L	H				
Meropenem 10 µg	H		H*				L	L	H		H	H	H	L	H	H	H	
Ciprofloxacin 5 µg	L				L		L	L					H	H*		L	L	
Norfloxacin 10 µg							L		L				H*	H				
Pefloxacin 5 µg			L	L	L		NA	NA	NA				H					
Gentamicin 10 µg					H		L		NA				H	H				
Tobramycin 10 µg	NA	NA	H										H*	H*				
Erythromycin 15 µg			L		L		L		L				H	H	L*	L		
Tetracycline 30 µg			L	L*	L*		L		L*					L	L		L	

These data were published on www.eucast.org in October 2015.

Mean value within ± 1 mm of the target value
Mean value >1 mm but within ± 2 mm of the target value
Mean value >2 mm from target value but still within the QC range
Mean value out of the QC range
Disk included in first study, but not supplied for second study

NA = Not Available

H = High, mean value > 1 mm above target

L = Low, mean value > 1 mm below target

* One or more readings out of QC range

Thank you

Acknowledgements

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Erika Matuschek, EUCAST Development Lab

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Mandy Wooton, Public Health Wales