NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

About EUCAST

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What is EUCAST?

- EUCAST is under the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the European Centre for Disease Prevention and Control (ECDC), a network of established experts in the determination of antimicrobial breakpoints and in antimicrobial susceptibility testing.

EUCAST objectives

- To determine, review and revise European clinical breakpoints and epidemiological cut-off values for surveillance of antimicrobial resistance in close collaboration with the European Medicines Agency (EMA) and ECDC.
- To promote the development and standardization of in-vitro antimicrobial susceptibility testing methods used in Europe.
- To promote quality assurance of in-vitro antimicrobial susceptibility testing.

Objectives continue

- To promote education and training in antimicrobial susceptibility testing.
- To advise ECDC and other European Union health agencies on issues related to antimicrobial susceptibility testing and detection of resistance determinants relevant to public health.
- To collaborate with international groups, ECDC and other European Union health agencies involved in antimicrobial susceptibility testing and/or the epidemiology of antimicrobial resistance in human pathogens.
- To work towards international consensus and harmonization of clinical breakpoints and antimicrobial susceptibility testing.

EUCAST breakpoints for new antimicrobial agents

- For new antimicrobial agents there is an agreement between the EMA, pharmaceutical industry and EUCAST with respect to breakpoint determination and is recognised as part of the official EMA process for approval of new antimicrobial agents (see EMA SOP/H/3043 14 February 2005, revised 23 January 2007).
- Only the applicant of the specific product under consideration will be part of the process, as outlined in the EMA SOP/H/3943.

Structure of EUCAST

- Steering Committee- decision making body
- General Committee
- Subcommittees
- National Antimicrobial Susceptibility Testing Committees (NAC)

EUCAST footprint

- Organised by ESCMID, ECDC and the national break point committees in Europe.
- Future: ”ECDC External Expert Committee” Steering committee, General committee (European reps), and Consultation network.
- Integrated part of EMEA process for approval of new antimicrobials(SOP).
- Advisors from EMEA and ECDC.
- Funding from ECDC and ESCMID.

EUCAST tasks

- Determine clinical breakpoints and epidemiological cutoffs for existing and new antimicrobials(bacteria, fungi).
- Provide standardised and harmonised methodology for AST in Europe (bacteria, fungi).
- Education of laboratory staff.
- Liaise with European regulatory organisations and NGOs and with international groups involved in breakpoints, methodology and surveillance of resistance.

European breakpoints harmonised!

- Harmonising break points for existing antibacterial drugs.
- All break points revised.
- Review process started–glycopeptides and carbapenems.

EUCAST breakpoint committee

Existing antimicrobials

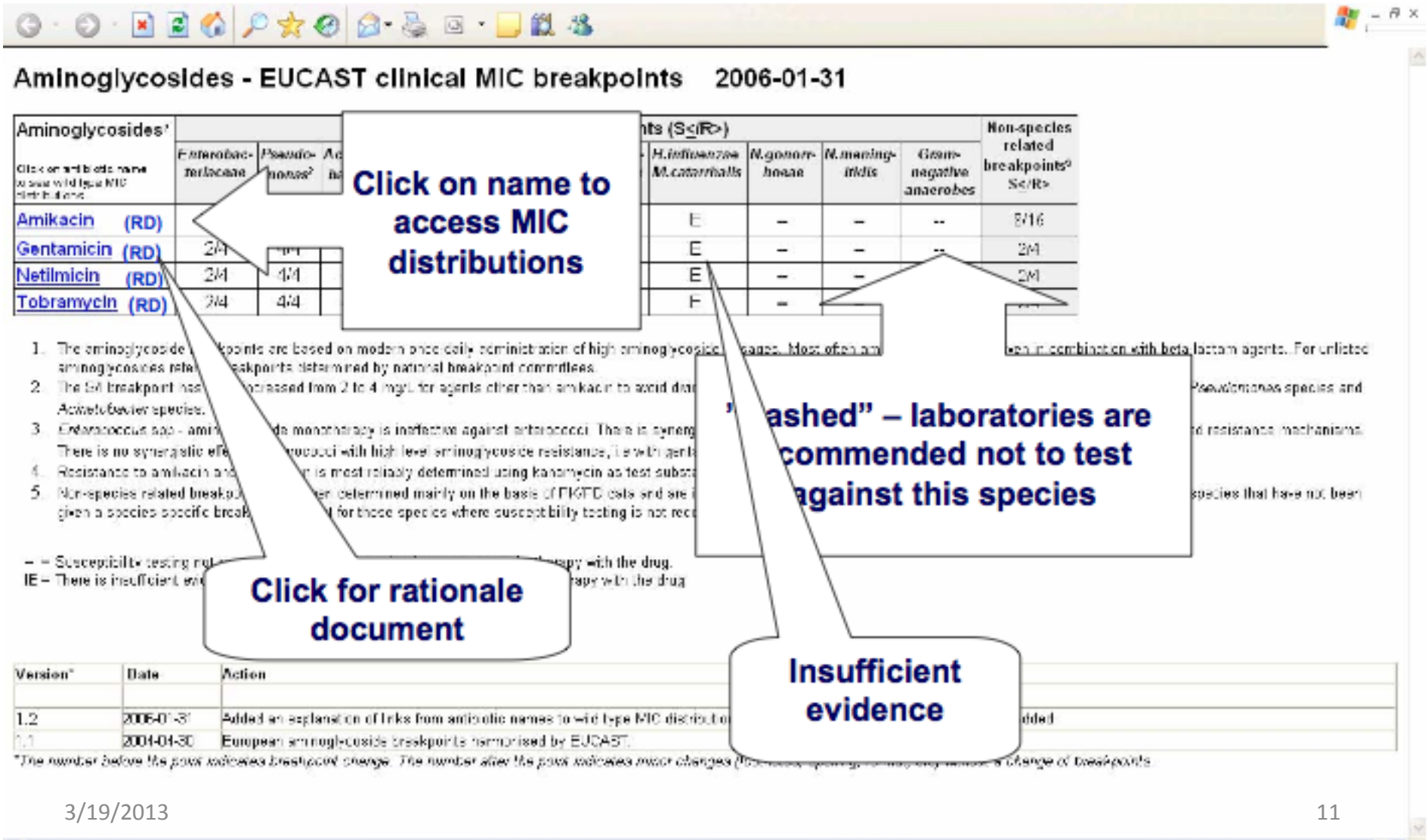
- Aminoglycosides
- Carbapenems& aztreonam
- Cephalosporins iv
- Cephalosporins oral
- Fluoroquinolones
- Glycopetides
- Macrolides and lincosamines
- Miscellaneous antimicrobials
- Penicillins
- Tetracyclines
- Antifungal drugs(flu-and voriconzole)

New drugs through EMEA

- Daptomycin
- Tigecycline
- Garenoxacin
- Doripenem
- Cefalosporine
- Glycopeptides
- Fluoroquinolone
- Diaminopyrimidine
- Extensions of indications

EMEA = European Medicines Agency

EUCAST breakpoint tables EUCAST breakpoint tables available at http://www.eucast.org



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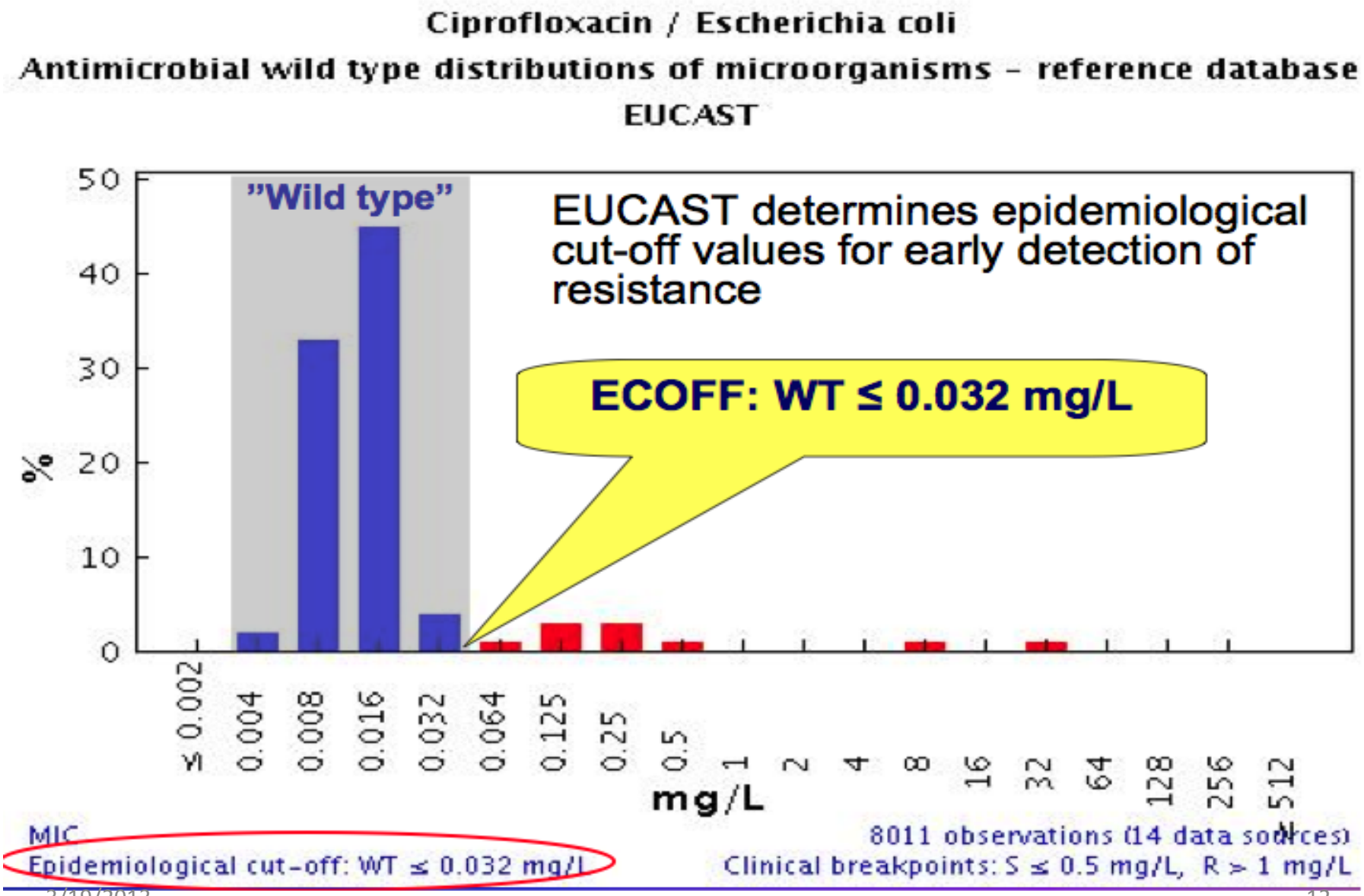
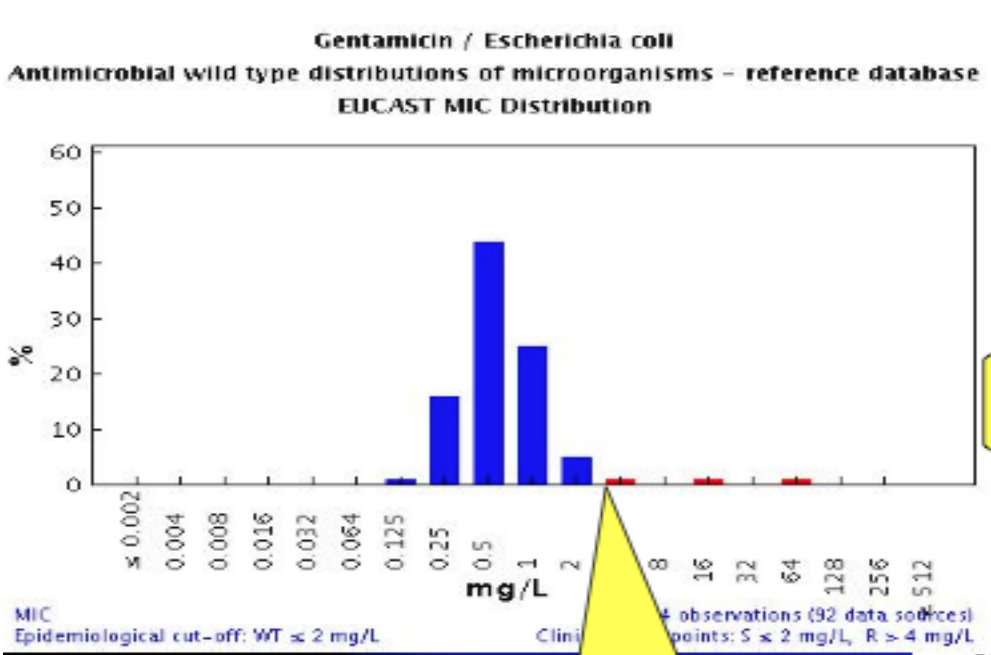
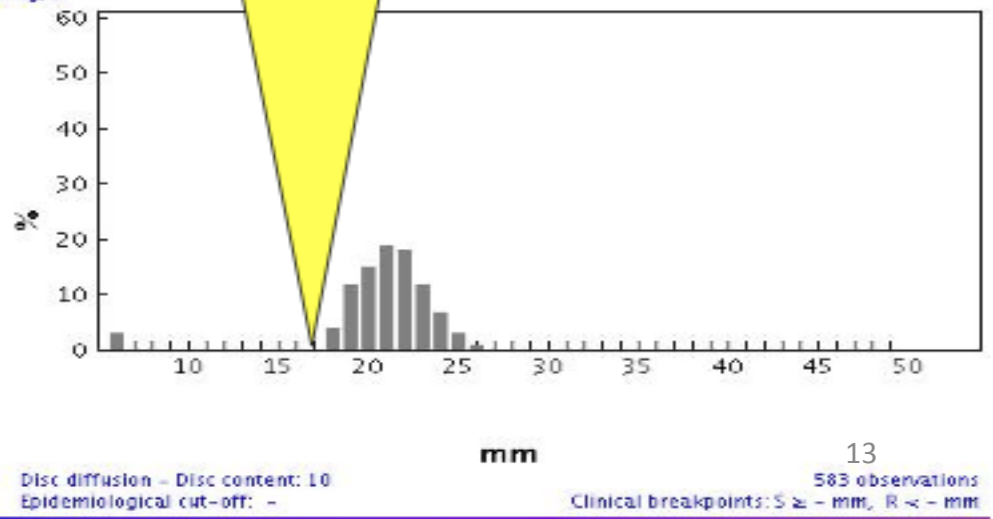

Ciprofloxacin / Escherichia coli
Antimicrobial wild type distributions of microorganisms – reference database EUCAST
"Wild type"
EUCAST determines epidemiological cut-off values for early detection of resistance
ECOFF: WT ≤ 0.032 mg/L
%
50
40
30
20
10
0
≤ 0.002
0.004
0.008
0.016
0.032
0.064
0.125
0.25
0.5
1
2
4
8
16
32
64
128
256
512
mg/L
MIC
Epidemiological cut-off: WT ≤ 0.032 mg/L
8011 observations (14 data sources)
Clinical breakpoints: S ≤ 0.5 mg/L, R > 1 mg/L

Cont.



ECOFF: WT ≤ 2 mg/L

ECOFF: WT ≤ 18 mm



EUCAST and CLSI are different

EUCAST

- Committee of representatives of national breakpoint committees and the medical profession in European countries.
- In dialogue with regulatory authorities (ECDC, EMEA).
- In consultation with industry.
- Consensus decisions , no vote.

CLSI

- Committee of representatives from the medical profession, science, industry and regulatory authorities.
- Decisions by vote.

EUCAST vs. CLSI

EUCAST

- Funded by ESCMID, ECDC and nationals breakpoint committees.
- Industry consultative role.
- Five meetings per year.
- EUCAST functions as the breakpoint committee of EMEA.
- Rationale documents published on EUCAST website for free.
- Clinical breakpoints and epidemiological cut-offs.

CLSI

- Funded by member-national (industry, government institutions, societies, laboratories) and sale of documents.
- Industry part of decision process.
- Two meetings per year.
- FDA determines breakpoints.
- CLSI was recognized by FDA from 2010.
- Breakpoints determined by FDA may be amended by CLSI after 2 yrs.
- Rationale for decisions not published in an organized fashion and for sale.
- Clinical breakpoints.

Disk tests from EUCAST and CLSI

EUCAST

- Mueller Hinton Inoculum 0.5 McF.
- Incubation 18 +/-2 h (24h for some organisms).
- MH+5% Horse Blood and 20 mg β-NAD for streptococci, pneumococci & *H. influenzae.*
- Disk strengths.
- QC strains and reference ranges.

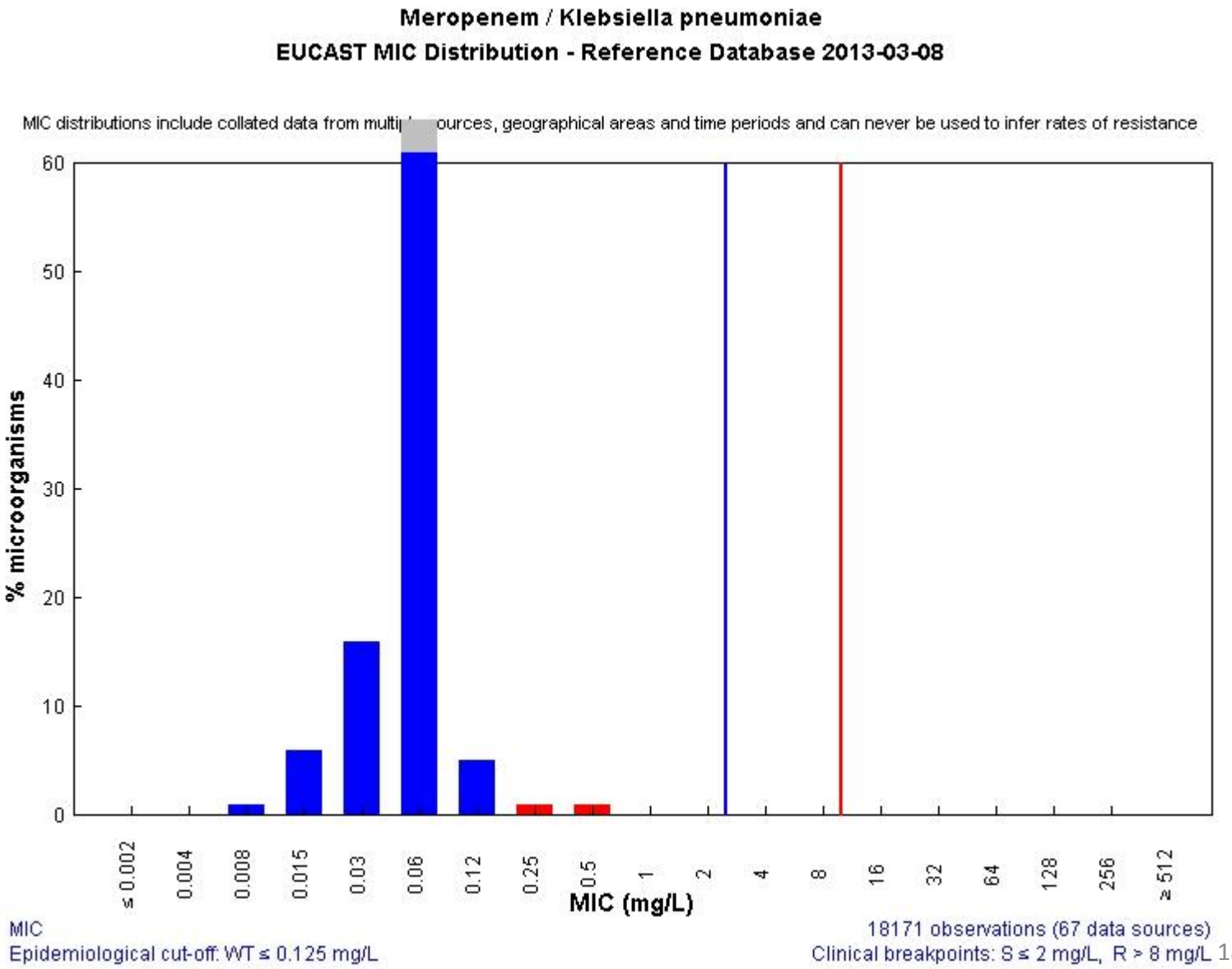
CLSI

- Mueller Hinton Inoculum 0.5 McF.
- Incubation 18 +/-2 h (24h for some organisms).
- Two different plates for fastidious organisms.
- Disk strengths.
- QC strains and reference ranges.

EUCAST and CLSI breakpoints are different example Enterobacteriaceae

Penicillins[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R >		S ≥	R <	
Benzylpenicillin	-	-		-	-	
Ampicillin	8[I]	8	10	14[A,B]	14[B]	1/A. Wild type Enterobacteriaceae are categorised as susceptible to aminopenicillins. Some countries prefer to categorise wild type isolates of *E. coli* and *P. mirabilis* as intermediate. When this is the case, use the MIC breakpoint S ≤ 0.5 mg/L and the corresponding zone diameter breakpoint S ≥ 50 mm. B. Ignore growth that may appear as a thin inner zone on some batches of Mueller-Hinton agars.
Ampicillin-sulbactam	8[1,2]	8[2]	10-10	14[A,B]	14[B]	2. For susceptibility testing purposes, the concentration of sulbactam is fixed at 4 mg/L.
Amoxicillin	8[I]	8	-	Note[C]	Note[C]	C. Susceptibility inferred from ampicillin.
Amoxicillin-clavulanate	8[1,3]	8[3]	20-10	17[A,B]	17[B]	3. For susceptibility testing purposes, the concentration of clavulanate is fixed at 2 mg/L.
Piperacillin	8	16	30	20	17	
Piperacillin-tazobactam	8[4]	16[4]	30-6	20	17	4. For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.
Ticarcillin	8	16	75	23	23	
Ticarcillin-clavulanate	8[3]	16[3]	75-10	23	23	
Phenoxymethylpenicillin	-	-		-	-	
Oxacillin	-	-		-	-	
Cloxacillin	-	-		-	-	
Dicloxacillin	-	-		-	-	
Flucloxacillin	-	-		-	-	
Mecillinam (uncomplicated UTI only)	8[E]	8[E]	10	15[E,F]	15[E, F]	E. Mecillinam (pivmecillinam) breakpoints relate to *E. coli*, *Klebsiella* spp. and *P. mirabilis* only. F. Ignore isolated colonies within the inhibition zone for *E. coli*.

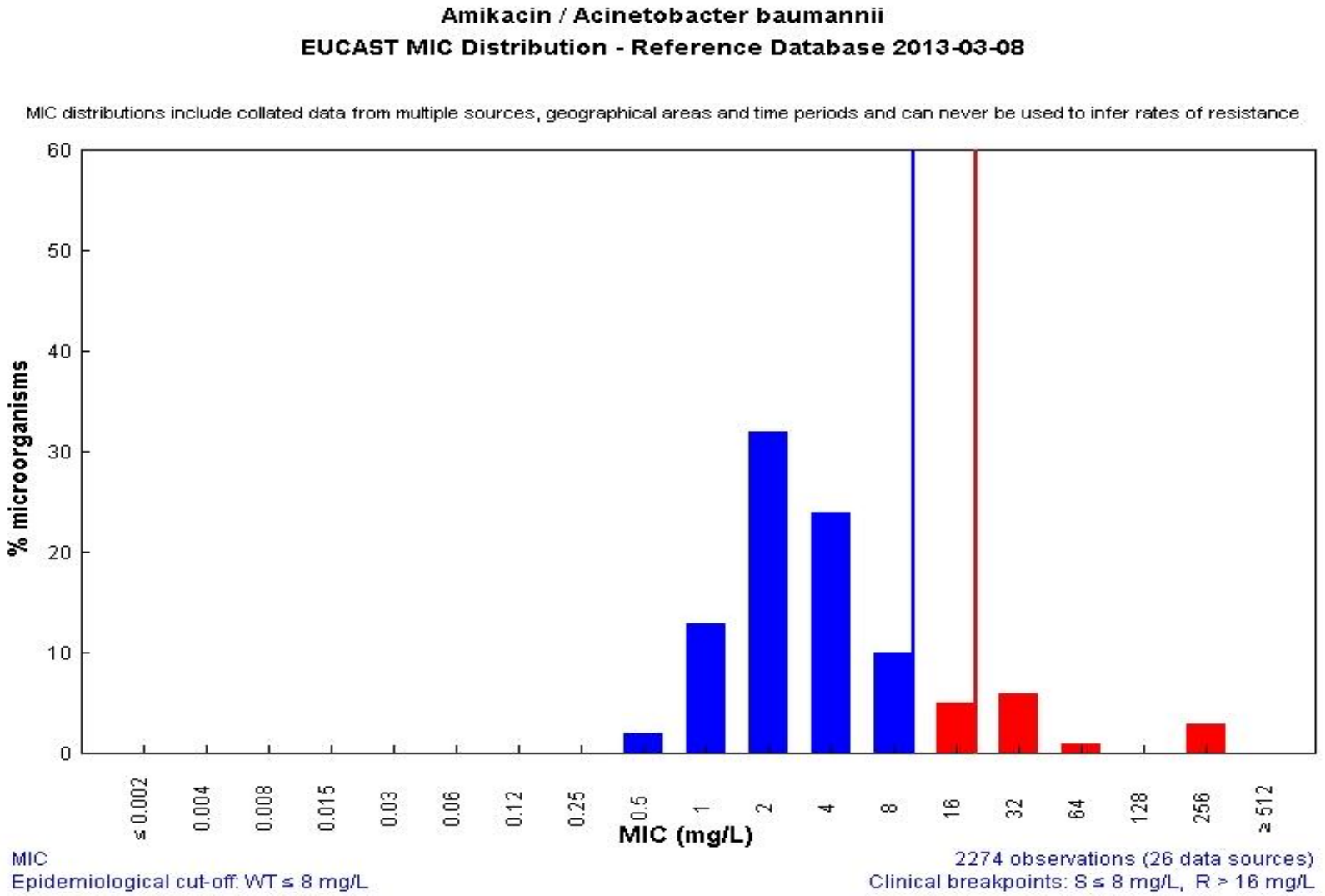
MIC distribution, example



EUCAST clinical breakpoints for carbapenems in Enterobacteriaceae

Carbapenems[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R >		S ≥	R <	
						1. The carbapenem breakpoints for Enterobacteriaceae will detect all clinically important resistance mechanisms (including the majority of carbapenemases). Some isolates that produce carbapenemase are categorised as susceptible with these breakpoints and should be reported as tested, *i.e.* the presence or absence of a carbapenemase does not in itself influence the categorisation of susceptibility. In many areas, carbapenemase detection and characterisation is recommended or mandatory for infection control purposes.
Doripenem	1	4	10	24	18	
Ertapenem	0.5	1	10	25	22	
Imipenem[2]	2	8	10	22	16	2. Low-level resistance is common in *Morganella* spp., *Proteus* spp. and *Providencia* spp.
Meropenem	2	8	10	22	16	

MIC distribution for *A. baumannii*



Implementation of EUCAST breakpoints

- MIC-testing of any kind
- National systems for disk diffusion from France, UK or Sweden
- Phoenix
- Vitek2, MicroScan–ongoing
- Disk diffusion – ongoing

Thank you for your attention!

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