Breakpoint, criteri interpretativi e nuovi antibiotici: cosa è cambiato?

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Rimini, 13 novembre 2017

Breakpoint tables for interpretation of MICs and zone diameters

Version 1.0 December 2009

Notes

1. The EUCAST tables of clinical breakpoints v. 1.0 contain clinical MIC breakpoints (determined over the period 2002-2009) and their inhibition zone diameter correlates. The latter are tentative for the period December 2009 - November 2010. During this period some additions will be made and the calibration between MICs and inhibition zone diameters may be refined on the basis of more extensive data that will be available in 2010.

European Committee on Antimicrobial Susceptibility Testing

Version 1.1 April 2010

Content	Page

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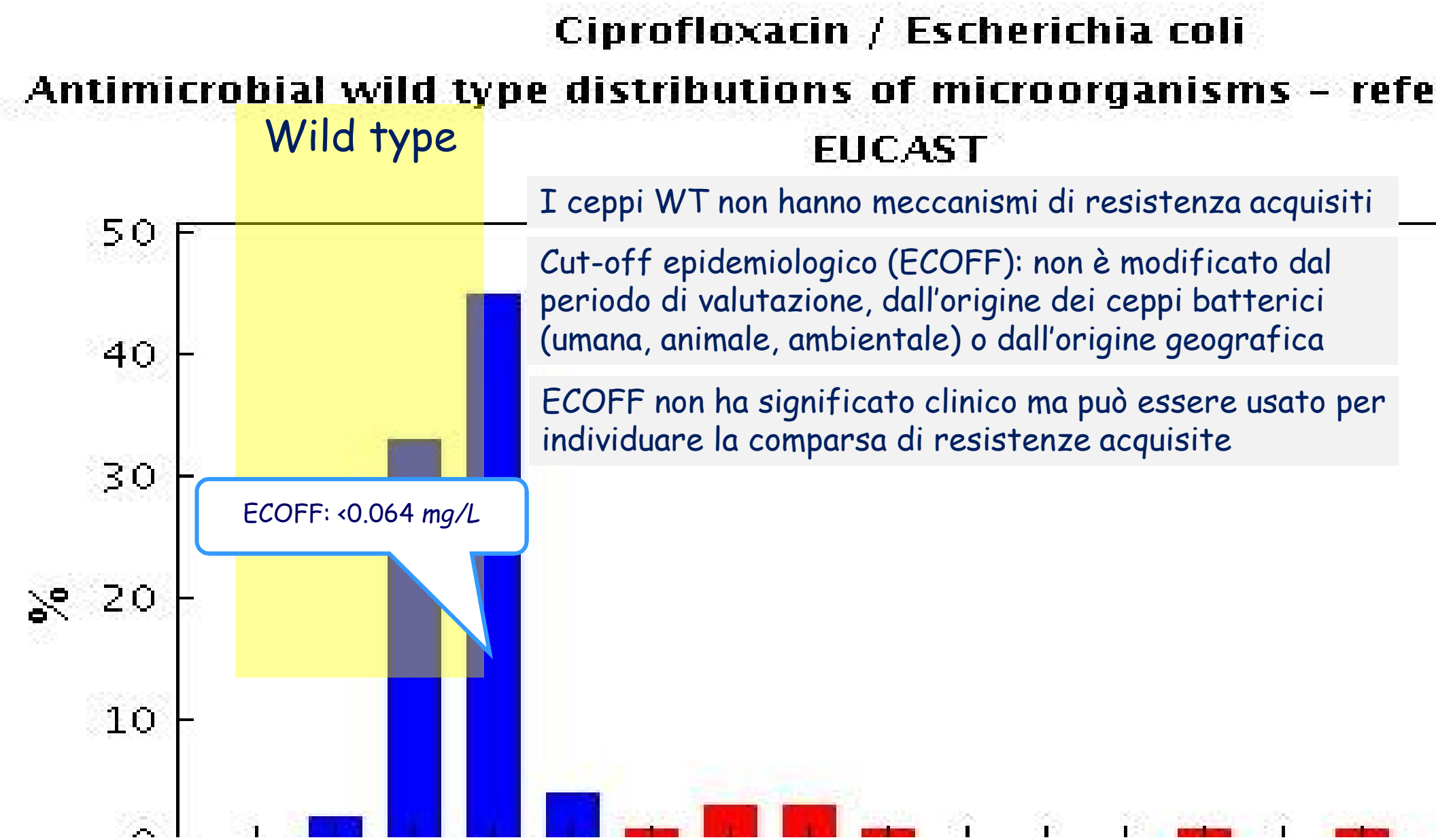
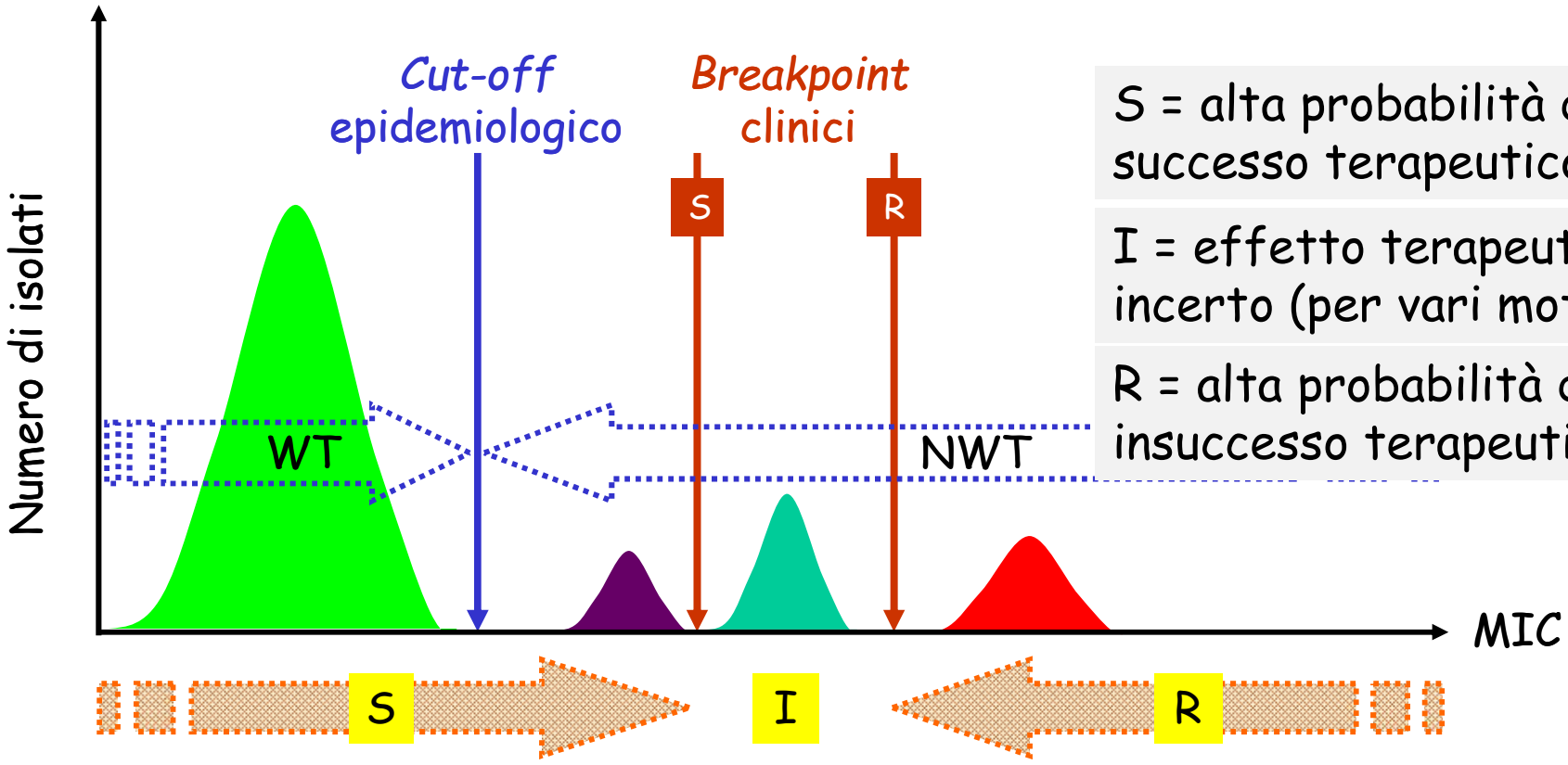


I ceppi WT non hanno meccanismi di resistenza acquisiti

Cut-off epidemiologico (ECOFF): non è modificato dal periodo di valutazione, dall'origine dei ceppi batterici (umana, animale, ambientale) o dall'origine geografica

ECOFF non ha significato clinico ma può essere usato per individuare la comparsa di resistenze acquisite

Sensibilità e resistenza
Valori di cut-off epidemiologico (ECOFF) e breakpoint clinici



S = alta probabilità di successo terapeutico

I = effetto terapeutico incerto (per vari motivi)

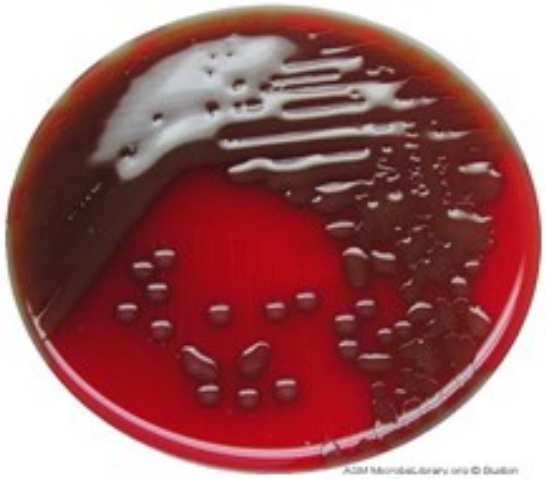
R = alta probabilità di insuccesso terapeutico

Attività antibatterica compensata dalla farmacocinetica del farmaco

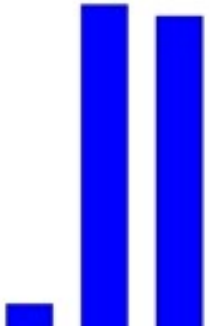
EUCAST: la dose conta …

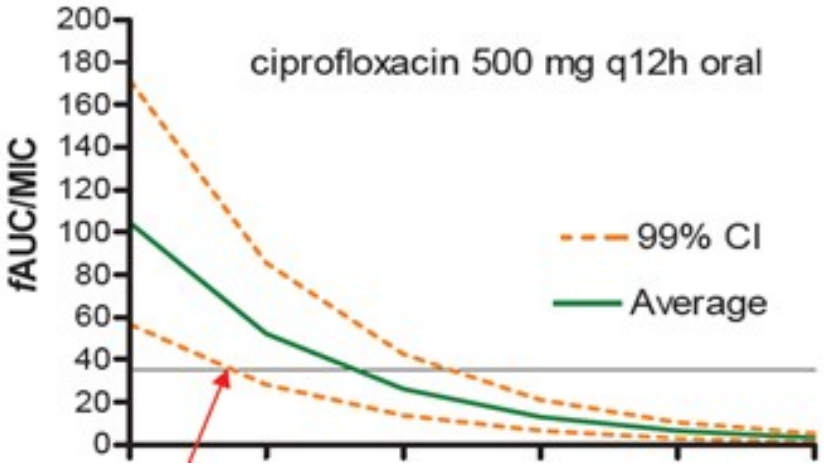
Microrganismo vs. antibiotico

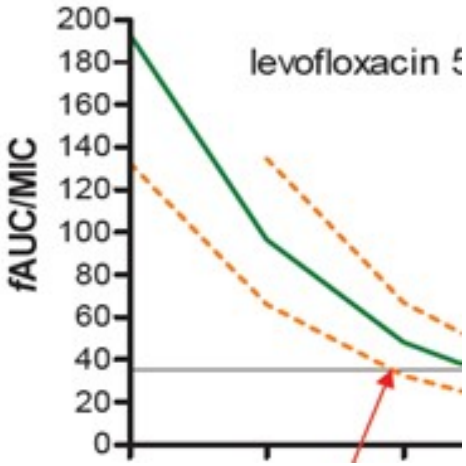
Dose somministrata



I *breakpoint* si applicano ai comuni dosaggi sulla base dei dati Pk:Pd *(rationale documents)*







EUCAST: categorie determinate sulla base dei *breakpoint clinici*

Sensibile (S)

Il livello di attività dell'antibiotico nei confronti del microrganismo è associato ad un'elevata probabilità di successo terapeutico.

Intermedio (I)

Il livello di attività dell'antibiotico nei confronti del microrganismo è associato ad un effetto terapeutico incerto.

Non è escluso che l'infezione possa essere trattata appropriatamente in distretti corporei in cui il farmaco è attivamente concentrato o utilizzando alti dosaggi.

La categoria intermedia rappresenta anche una zona cuscinetto che potrebbe evitare che modesti ma difficilmente controllabili fattori tecnici possano causare importanti discrepanze interpretative.

Resistente (R)

Il livello di attività dell'antibiotico nei confronti del microrganismo è associato ad un'elevata probabilità di fallimento terapeutico.

Proposed modifications to EUCAST definition of the intermediate category

Background
The original EUCAST definition included the various traditional uses of the intermediate category:

"A microorganism is defined as intermediate by a level of antimicrobial agent activity associated with uncertain therapeutic effect. It implies that an infection due to the isolate may be appropriately treated in body sites where the drugs are physiologically concentrated or when a high dosage of drug can be used; it also indicates a buffer zone that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations."

Detailed below are proposals to modify EUCAST definition of the intermediate category. The proposals are open for comment by 3 December 2015.

Le modificazioni proposte rimuovono dalla definizione di categoria di sensibilità intermedia il concetto di una zona tampone tecnica.

Proposed modifications to EUCAST definition of the intermediate category

The following proposed revised definitions remove the concept of a technical buffer zone from the definition of intermediate category and include some typographical changes.

Definitions of clinical breakpoints and the epidemiological cut-off value

1. Clinical breakpoints

Un microrganismo è definito come sensibile se ha un livello di attività antimicrobica associato con una alta probabilità di successo terapeutico

Un microrganismo è definito come intermedio se ha un livello di attività antimicrobica associato con una alta probabilità di successo terapeutico ma solo quando può essere usato un dosaggio più alto rispetto a quello normale o quando l'agente si concentra fisiologicamente nel sito dell'infezione.

Un microrganismo è definito come resistente se ha un livello di attività antimicrobica associato con una alta probabilità di fallimento terapeutico

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Proposed modifications to EUCAST definition of the intermediate category

Proposed modifications to EUCAST definitio
Intermediate category
2nd consultation 2017

In 2015, EUCAST proposed to change the definition of the Intermediate catego
consultation generated numerous comments from colleagues (see the EUCAS
http://www.eucast.org/documents/consultations/).

Conclusion of the consultation: The detailed and perceptive comments are a
However, the current definition remains unsatisfactory since it harbours four dif
interpretations, but no indication to the clinician as to which interpretation applie
cases.
EUCAST has only rarely used intermediate as "a buffer zone", an area betwee
avoid major and very major errors, and has rarely used the Intermediate catego
increased exposure of the organism to the agent can be achieved (by adjusting

Proposed modifications to EUCAST definition of the intermediate category

2) Reserve the designation "I - intermediate" for measureme only.

Proposed new definition:
Intermediate (I): A microorganism is defined as intermediate by a antimicrobial activity associated with an uncertain effect due to a susceptibility testing results within the area of technical uncertair

The intermediate definition should be clarified regarding how the be handled by the laboratory prior to reporting according to the ir

Sincerely

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Rimini, 13 novembre 2017

Proposed modifications to EUCAST definition of the intermediate category

Iztok Štrumbelj on behalf of Slovenian National Antimicrobial Susceptibility Testing Committee (SKUOPZ)	**1a. We propose different symbol instead of "I" (one letter c abbreviation of intermediate category if new definition will** We think that: letter "I" in SIR is associated with different meani difficult to associate new meanings with old symbol. In any case, intense communication with clinicians will be nece definition is adopted. However, if we start to use new symbol /

Possible options for replacement of "I" (other options may be used):

- S^H
- SH
- S_H
- H

1.b. We propose that short legend to the abbreviation is determined by EUCAST. e.g.:

SH (or H or S or...) – sensitive by adjusting the dosing regimen to enhance exposure, or if the antimicrobial agent is concentrated at the site of infection.*

Or something shorter, if possible (e.g. high dosing).

Table 2A-1
Enterobacteriaceae
M02 and M07

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints (nearest whole mm)				Interpretive Categories and MIC Breakpoints (µg/mL)				
			S	SDD	I	R	S	SDD	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)											
U	Cefazolin	30 µg	≥15	–	–	≤14	≤16	–	–	≥32	**(11) Bu** for the *E. coli* **Breakp** regime See a CEPHI
C	Ceftaroline	30 µg	≥23	–	20–22	≤19	≤0.5	–	1	≥2	**(12) Bu** regime
B	Cefepime	30 µg	≥25	19–24	–	≤18	≤2	4–8	–	≥16	**(13)** T based 12 h. on dos cefepir or mo approv See A about Also s

European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs and zone diameters

Version 7.1, valid from 2017-03-10

Rimini, 13 novembre 2017

Enterobacteriaceae

EUCAST Clinical Breakpoint Tables v. 7.1, valid from 2017-03-10

Miscellaneous agents	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Chloramphenicol	8	8	30	17	17
Colistin[1]	2	2		Note[A]	Note[A]
Daptomycin	-	-		-	-
Fosfomycin iv	32[2]	32[2]	200[B]	24[C,D]	24[C,D]
Fosfomycin oral (uncomplicated UTI only)	32[2]	32[2]	200[B]	24[C,D]	24[C,D]
Fusidic acid	-	-		-	-
Metronidazole	-	-		-	-
~~Mupirocin~~					
Nitrofurantoin (uncomplicated UTI only), *E. coli*	64	64	100	11	11
Nitroxoline (uncomplicated UTI only), *E. coli*	16	16	30	15	15
Rifampicin	-	-		-	-
Spectinomycin	-	-		-	-
Trimethoprim (uncomplicated UTI only)	2	4	5	18	15
Trimethoprim-sulfamethoxazole[3]	2	4	1.25-23.75	14	11

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Enterobacteriaceae

EUCAST Clinical Breakpoint Tables v. 7.1, valid from 2017-03-10

Notes

Numbered notes relate to general comments and/or MIC breakpoints.
Lettered notes relate to the disk diffusion method.

1. Quality control of colistin must be performed with both a susceptible QC strain (*E. coli* ATCC 25922 or *P. aeruginosa* ATCC 27853) and the colistin resistant *E. coli* NCTC 13846 (*mcr-1* positive).
2. Agar dilution is the reference method for fosfomycin. MICs must be determined in the presence of glucose-6-phosphate (25 mg/L in the medium). Follow the manufacturers' instructions for commercial systems.
3. Trimethoprim:sulfamethoxazole in the ratio 1:19. Breakpoints are expressed as the trimethoprim concentration.

A. Use an MIC method.
B. Fosfomycin 200 µg disks must contain 50 µg glucose-6-phosphate.
C. Zone diameter breakpoints apply to *E. coli* only. For other Enterobacteriaceae, use an MIC method.
D. Ignore isolated colonies within the inhibition zone (**see pictures below**).

Examples of inhibition zones for *Escherichia coli* with fosfomycin.
a-c) Ignore all colonies and read the outer zone edge.
d) Record as no inhibition zone.

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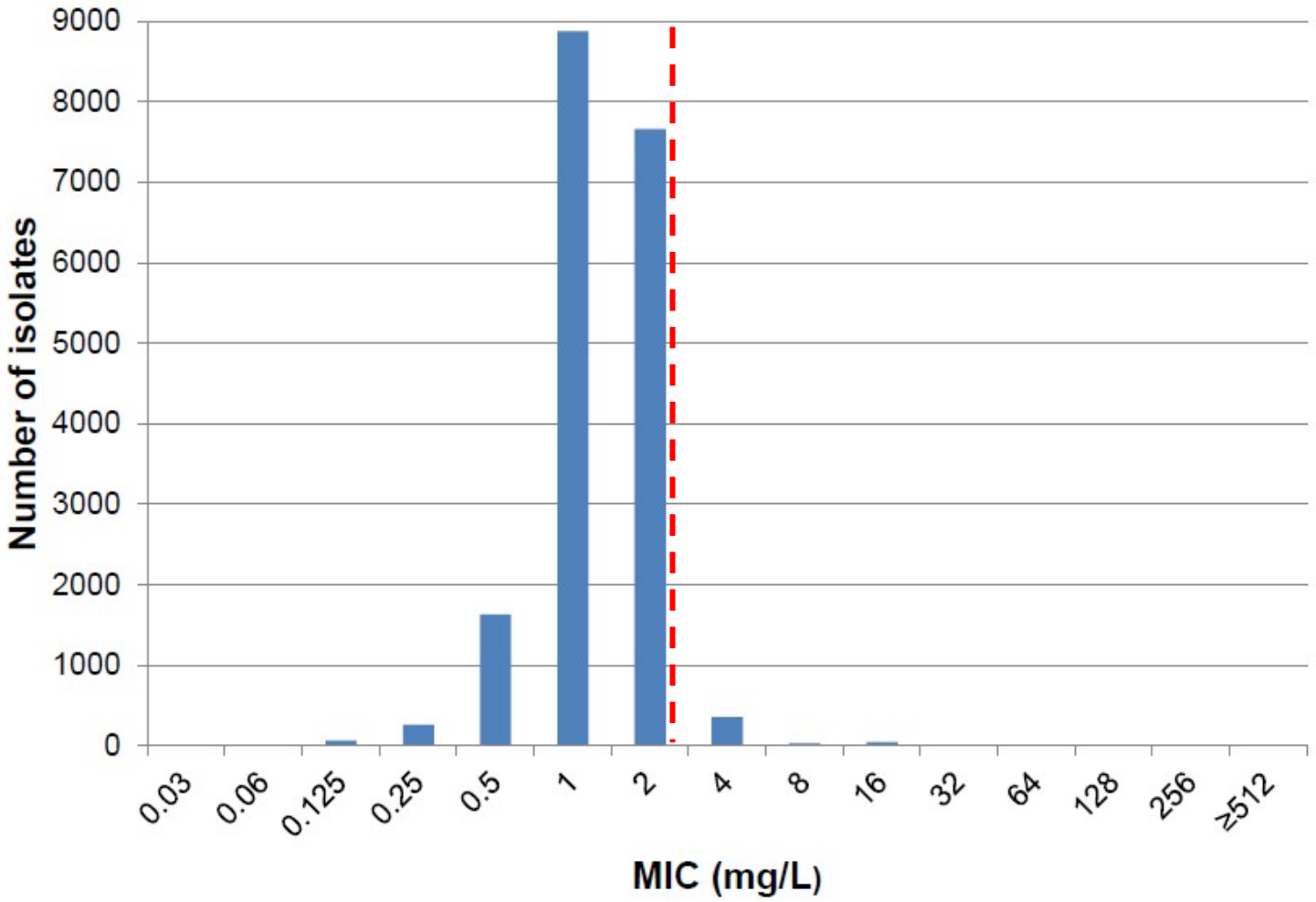
Consultation on proposal to reduce colistin breakpoints for *Pseudomonas aeruginosa* to susceptible ≤2 mg/L, resistant > 2 mg/L



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Proposed modification of fluoroquinolone br

Background

Fluoroquinolone breakpoints were set a decade ago and were a compromise between the microbiological, pharmacokinetic-pharmacodynamic (PK-PD) and clinical data available at the time and the compromises to achieve harmonization of breakpoints. Over the last few years more information has become available and review of the breakpoints is warranted. The procedure for revision is as stated in EUCAST SOP3 on review and revision of breakpoints (http://www.eucast.org/documents/sops/). The process for assessment of data was essentially:

1. Pharmacodynamic targets were determined for fluoroquinolones as a class.

2. Monte Carlo simulations were performed for each of the compounds.

3. Probabilities of target attainment were evaluated.

4. PK-PD breakpoints were set.

5. Clinical breakpoints were set based on the PK-PD breakpoints and taking into account the requirement to avoid splitting wild type (WT) distributions and clinical data relating MIC to outcome, if available.

Enterobacteriac

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

Fluoroquinolones	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Ciprofloxacin	0.25	0.5	5
Ciprofloxacin, *Salmonella* spp.[1]	0.06	0.06	
Pefloxacin (screen), *Salmonella* spp.[1]	NA	NA	5
Levofloxacin	0.5	1	5
Moxifloxacin	0.25	0.25	5
Nalidixic acid (screen)	NA	NA	

Pseudomonas s

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

Fluoroquinolones	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Ciprofloxacin[1]	0.5	0.5	5
Levofloxacin[2]	1	1	5
Moxifloxacin	-	-	
Nalidixic acid (screen)	NA	NA	

Miscellaneous agents	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Chloramphenicol	-	-	

Acinetobacter s

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

Fluoroquinolones	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Ciprofloxacin[1]	1	1	5
Levofloxacin	0.5	1	5
Moxifloxacin	-	-	
Nalidixic acid (screen)	NA	NA	

Miscellaneous agents	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Chloramphenicol	-	-	

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Streptococcus pneum

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

Fluoroquinolones	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Ciprofloxacin	-	-	
Levofloxacin[1]	2	2	5
Moxifloxacin	0.5	0.5	5
Nalidixic acid (screen)	NA	NA	
Norfloxacin (screen)	NA	NA	10

Staphylococcus

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

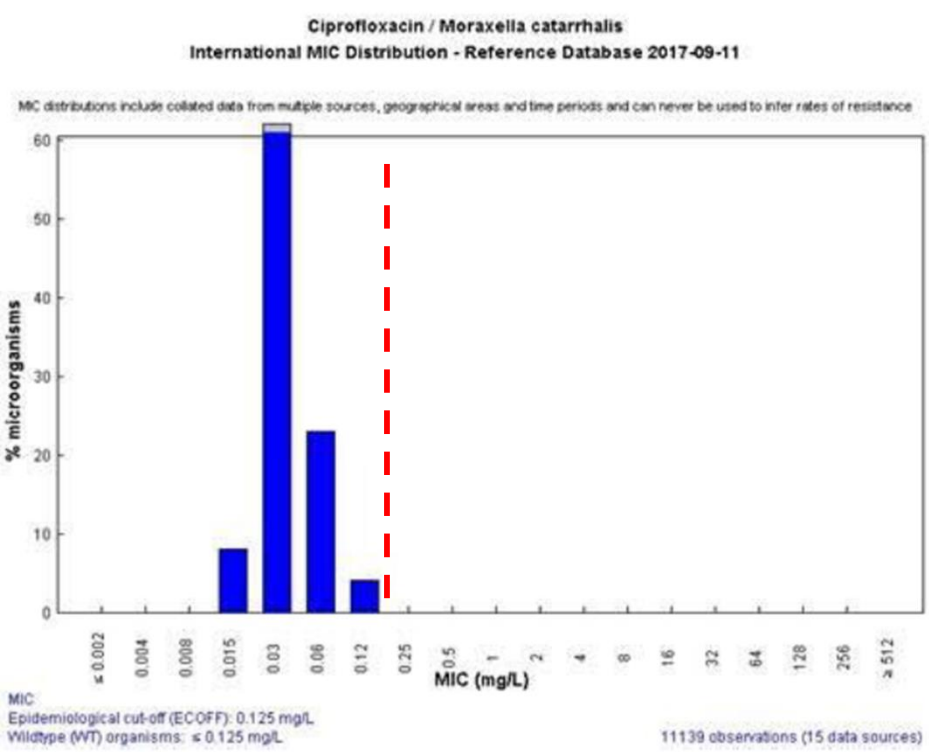
Fluoroquinolones[1]	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Ciprofloxacin[2], *S. aureus*	1	1	5
Ciprofloxacin[2], Coagulase-negative staphylococci	1	1	5
Levofloxacin, *S. aureus*	1	1	5
Levofloxacin, Coagulase-negative staphylococci	1	1	5
Moxifloxacin, *S. aureus*	0.25	0.25	5
Moxifloxacin, Coagulase-negative staphylococci	0.25	0.25	5
Nalidixic acid (screen)	NA	NA	

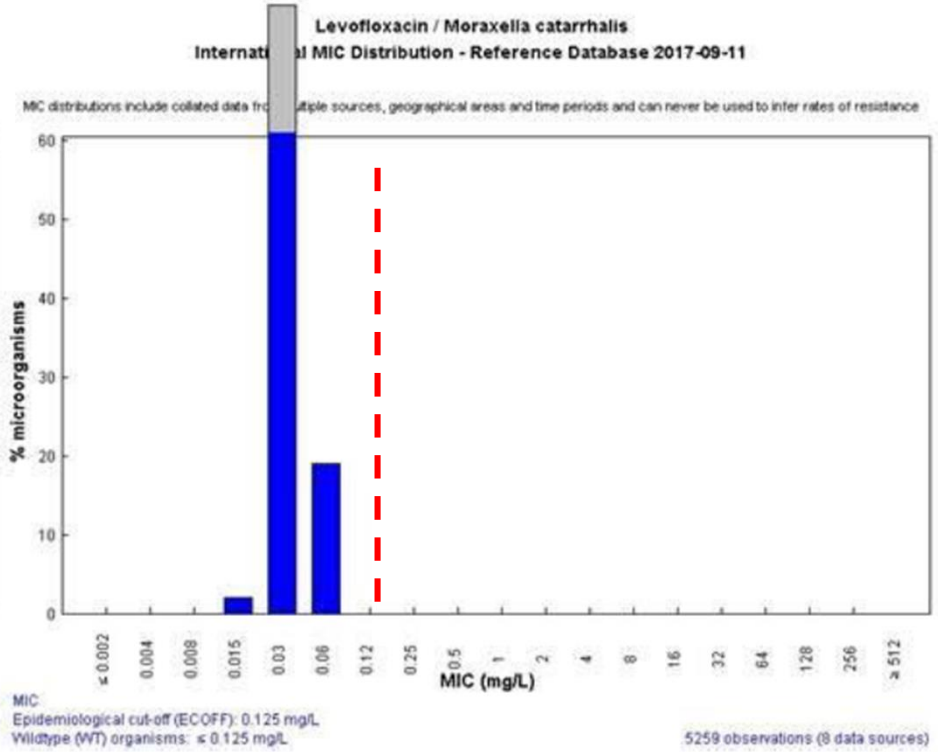
Proposed fluoroquinolone breakpoints for *Moraxella catarrhalis*

Breakpoint Committee Consultation, October 2017

Ciprofloxacina

Levofloxacina



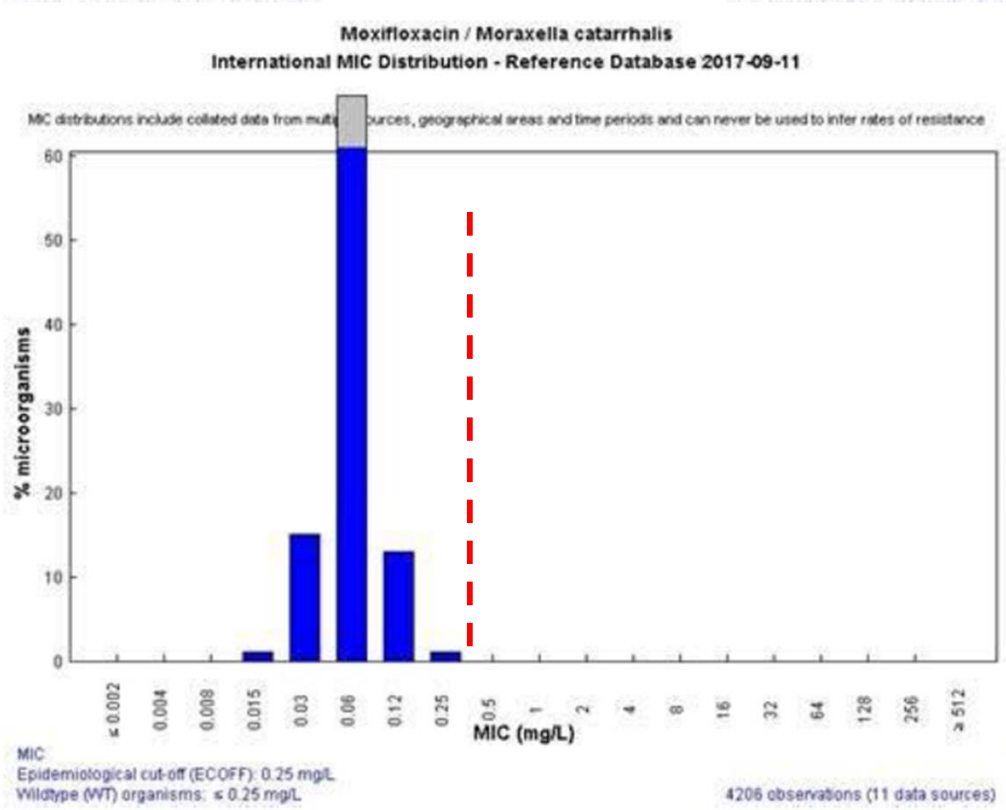


Rimini, 13 novembre 2017

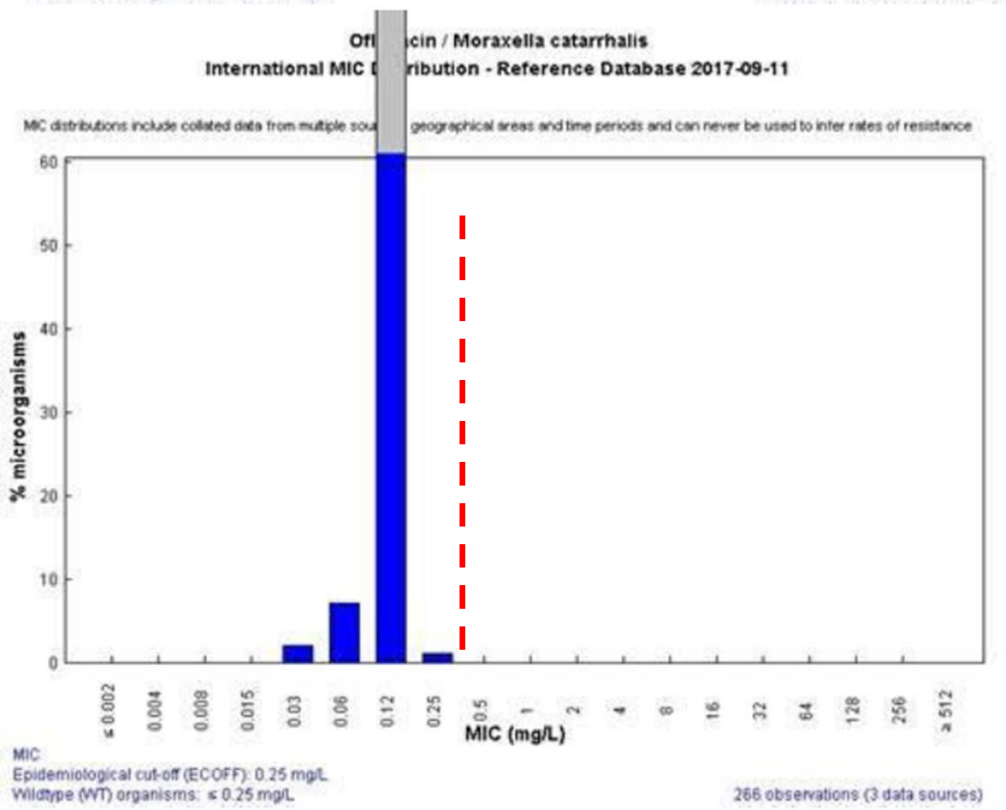
Proposed fluoroquinolone breakpoints for *Moraxella catarrhalis*

Breakpoint Committee Consultation, October 2017

Moxifloxacina



Ofloxacina



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Proposed fluoroquinolone breakpoints for *Moraxella catarrhalis*

Breakpoint Committee Consultation, October 2017

Breakpoint proposti

Fluoroquinolones	MIC breakpoint (mg/L)	
	S ≤	R >
Ciprofloxacin	0.125	0.125
Levofloxacin	0.125	0.125
Moxifloxacin	0.25	0.25
Nalidixic acid (screen)	NA	NA
Norfloxacin (uncomplicated UTI only)	-	-
Ofloxacin	0.25	0.25

Breakpoint attuali

Fluoroquinolones	MIC breakpoint (mg/L)	
	S ≤	R >
Ciprofloxacin	0.5	0.5
Levofloxacin	1	1
Moxifloxacin	0.5	0.5
Norfloxacin (uncomplicated UTI only)	-	-
Ofloxacin	0.5	0.5

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Proposal to remove macrolide breakpoints for *Haemophilus influenzae* but include a note on possible clinical efficacy and ECOFFs to distinguish wild type from isolates with acquired resistance

Gli isolati di *H. influenzae* sono attualmente categorizzati come intermedi ai macrolidi con un range di MIC molto ampio. Con il programmato passaggio ad una nuova definizione di intermedio questa categorizzazione presto non sarà più appropriata.

H. influenzae MIC distributions from EUCAST MIC distribution website

Agent	MIC (mg/L)													ECOFF ≤ (mg/L)
	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	≥128	
Azithromycin	0	64	299	887	5442	15658	8888	1181	118	354	37	8	24	4
Clarithromycin	0	2	9	112	72	229	1192	6679	14779	4258	418	52	44	32
Erythromycin	1	7	21	113	127	618	4500	15097	7781	808	100	22	31	16
Roxithromycin	0	0	0	0	0	1	0	12	68	91	19	3	0	ND*
Telithromycin	6	4	16	54	279	1846	2662	486	38	14	2	5	0	8

*No ECOFF was originally designated as data were sparse. Current data suggest that be 4-64 mg/L and the ECOFF 64 mg/L.

Current Intermediate range is highlighted in yellow

Proposal to remove macrolide breakpoints for *Haemophilus influenzae* but include a note on possible clinical efficacy and ECOFFs to distinguish wild type from isolates with acquired resistance

It is proposed that macrolide breakpoints for *H. influenzae* are removed and notes added about problems of relating MICs to outcomes in a traditional way. In the table we will also add ECOFFs to distinguish isolates with acquired resistance from those belonging to the wild type.

Si propone che i breakpoint dei macrolidi per *H. influenzae* siano rimossi e sia aggiunta una nota riguardo al problema di correlare le MIC all'outcome in modo tradizionale. Verranno indicati gli ecoff per distinguere gli isolati con resistenza acquisita da quelli appartenenti ai wild-tipe.

Proposed Note for the Breakpoint Table (version 8.0)

Clinical evidence for the efficacy of macrolides in H. influenzae *respirat*
conflicting due to high spontaneous cure rates. Should there be a need
macrolide against this species, the epidemiological cut-offs (ECOFFs) s
detect strains with acquired resistance. The ECOFFs for each agent are
mg/L, clarithromycin 32 mg/L, erythromycin 16 mg/L and telithromycin 8

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FDA Approved Drugs for Infections and Infectious Diseases

Infections and Infectious Diseases

Dalvance (dalbavancin); Durata Therapeutics; For the treatment of acute bacterial skin and skin structure infections, Approved May 2014

Sivextro (tedizolid phosphate) ; Cubist Pharmaceuticals; For the treatment of acute bacterial skin and skin structure infections, Approved June 2014

Orbactiv (oritavancin); The Medicines Company; For the treatment of acute bacterial skin and skin structure infections, Approved August 2014

Zerbaxa (ceftolozane + tazobactam) ; Cubist Pharmaceuticals; For the treatment of complicated intra-abdominal and urinary tract infections, Approved December 2014

Avycaz (ceftazidime-avibactam); Actavis; For the treatment of complicated intra-abdominal and urinary tract infections, Approved February 2015

Baxdela (delafloxacin) tablets and injection; Melinta Therapeutics; For the treatment of acute bacterial skin and skin structure infections, Approved June 2017

Vabomere (meropenem and vaborbactam); The Medicines Company; For the treatment of complicated urinary tract infections , Approved August 2017

Advances in antibiotic therapy in the critically ill

Jean-Louis Vincent[1*], Matteo Bassetti[2], Bruno François[3], George Karam[4], Jean Chastre[5], Antoni Torres[6], Jason A. Roberts[7], Fabio S. Taccone[1], Jordi Rello[8], Thierry Calandra[9], Daniel De Backer[10], Tobias Welte[11] and Massimo Antonelli[12]

Table 2 The most important new antibiotic agents in the pipeline

Drug class	Drug name	Development phase	Potential indications
Lipopeptide and glycopeptide	Oritavancin	Approved August 2014	Acute bacterial skin and skin structure infections
Glycopeptide-cephalosporin heterodimer	TD-1607	Phase 1	Serious Gram-positive bacterial infections (acute bacterial skin and skin structure infections, hospital-acquired pneumonia/ventilator-associated pneumonia, bacteremia)
	TD-1792	Phase 2	Acute bacterial skin and skin structure infections, other serious infections caused by Gram-positive bacteria, including hospital-acquired pneumonia/ventilator-associated pneumonia and bacteremia
Lipo-glycopeptide	Dalbavancin	Approved May 2014	Acute bacterial skin and skin structure infections
	Ramoplanin	Phase 2	*Clostridium difficile*-associated diarrhea
Lipopeptide	Surotomycin	Phase 3	*Clostridium difficile*-associated diarrhea

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Table 2 The most important new antibiotic agents in the pipeline

Drug class	Drug name	Development phase	Potential indications
Oxazolidinone	Tedizolid	Approved June 2014	Acute bacterial skin and skin structure infections, hospital-acquired bacterial pneumonia/ventilator acquired bacterial pneumonia
	Cadazolid (quinolonyl-oxalidinone)	Phase 3	*Clostridium difficile*-associated diarrhea
	Radezolid	Phase 2	Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia
	MRX-I	Phase 1	Bacterial infections including community-acquired MRSA and vancomycin-resistant enterococci infections
	LCB01-0371	Phase 1	Bacterial infections

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Table 2 The most important new antibiotic agents in the pipeline

Drug class	Drug name	Development phase	Potential indications
Cephalosporin	GSK-2696266	Phase 1	Bacterial infections
Novel cephalosporin + β-lactamase inhibitor	Ceftolozane + tazobactam	Approved March 2015	Complicated urinary tract infections, complicated intra-abdominal infections, acute pyelonephritis (kidney infection), hospital-acquired bacterial pneumonia/ventilator associated pneumonia
	Ceftaroline + avibactam	Phase 2	Complicated urinary tract infections
	Ceftazidime + avibactam (CAZ-AVI)	Approved 2015	Complicated urinary tract infections, complicated intra-abdominal infections, acute pyelonephritis (kidney infection), hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia
Monobactam + novel β-lactamase inhibitor	Aztreonam + avibactam (ATM-AVI)	Phase 1	Bacterial infections
Carbapenem + novel β-lactamase inhibitor	Carbavance	Phase 1	Complicated urinary tract infections, complicated intra-abdominal infections, hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia, febrile neutropenia
	MK-7655 + imipenem/cilastatin	Phase 2	Complicated urinary tract infections, acute pyelonephritis, complicated intra-abdominal infections

Vincent *et al. Critical Care* (2016) 20:133

Advances in antibiotic therapy in the critically ill

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Table 2 The most important new antibiotic agents in the pipeline

Drug class	Drug name	Development phase	Potential indications
Macrolide			
Ketolide	Solithromycin	Phase 3	Community-acquired bacterial pneumonia, uncomplicated urogenital gonorrhea
LptD inhibitor	POL7080	Phase 2	Ventilator-associated bacterial pneumonia, low respiratory infections
Tetracycline	Omadacycline	Phase 2	Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections, complicated urinary tract infections
	Eravacycline	Phase 3	Complicated intra-abdominal infections, complicated urinary tract infections, hospital-acquired bacterial pneumonia
Monosulfactam	BAL30072	Phase 1	Multidrug-resistant Gram-negative bacterial infections
FabI inhibitor	Debio 1452	Phase 2	Acute bacterial skin and skin structure infections
	Debio 1450 (Debio 1452 pro-drug)	Phase 1	Bacterial infections
	CG-400549	Phase 2	Acute bacterial skin and skin structure infections; osteomyelitis

Vincent *et al. Critical Care* (2016) 20:133

Advances in antibiotic therapy in the critically ill

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Table 2 The most important new antibiotic agents in the pipeline

Drug class	Drug name	Development phase	Potential indications
Aminoglycoside	Plazomicin	Phase 3	Bloodstream infections and nosocomial pneumonia caused by carbapenem-resistant Enterobacteriaceae
Fluoroquinolone	WKC 771	Phase 1	Bacterial infections
	WKC 2349 (WCK 771 pro-drug)	Phase 1	Bacterial infections
	Avarofloxacin	Phase 2	Community-acquired bacterial pneumonia, acute bacterial skin and skin structure infections
	Finafloxacin	Phase 2	Complicated urinary tract infections, acute pyelonephritis (kidney infection), acute intra-abdominal infections, acute bacterial skin and skin structure infections
	Nemonoxacin	Phase 2	Community-acquired bacterial pneumonia, diabetic foot infection, acute bacterial skin and skin structure infections
	Zabofloxacin	Phase 2	Community-acquired bacterial pneumonia
	Delafloxacin	Phase 3	Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia, uncomplicated gonorrhea

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Table 2 The most important new antibiotic agents in the pipeline

Drug class	Drug name	Development phase	Potential indications
LpxC inhibitor	ACHN-975	Phase 1	Bacterial infections
DNA gyrase inhibitor	AZD0914	Phase 1	Uncomplicated gonorrhea
Methionyl-tRNA synthetase (MetRS) inhibitor	CRS-3123	Phase 1	*C. difficile* infection
Peptide deformylase inhibitor	GSK-1322322	Phase 2	Acute bacterial skin and skin structure infections
Type 2 topoisomerase inhibitor	GSK-2140944	Phase 2	Respiratory tract infections, acute bacterial skin and skin structure infections
Bicyclolide	EDP-788	Phase 1	Bacterial infections
Pleuromutilin	Lefamulin (BC-3781)	Phase 2	Acute bacterial skin and skin structure infections, community-acquired bacterial pneumonia
Elongation factor inhibitor	LFF571	Phase 2	*C. difficile*-associated diarrhea
Fusidane	Taksta (fusidic acid)	Phase 2	Prosthetic joint infections
Defensin-mimetic	Brilacidin	Phase 2	Acute bacterial skin and skin structure infections
	SMT19969	Phase 2	*C. difficile*-associated diarrhea

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Staphylococcus spp.

EUCAST Clinical Breakpoint Tables v. 7.1, valid from 2017-03-10

Glycopeptides and lipoglycopeptides[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Dalbavancin[2]	0.125[3.4]	0.125[3]		Note[A]	Note[A]
Oritavancin, *S. aureus*[2]	0.125[3.4]	0.125[3]		Note[A]	Note[A]
Teicoplanin, *S. aureus*[2]	2	2		Note[A]	Note[A]
Teicoplanin, Coagulase-negative staphylococci[2]	4	4		Note[A]	Note[A]
Telavancin, MRSA[2]	0.125[3.5]	0.125[3]		Note[A]	Note[A]
Vancomycin, *S. aureus*[2]	2	2		Note[A]	Note[A]
Vancomycin, Coagulase-negative staphylococci[2]	4	4		Note[A]	Note[A]
Oxazolidinones	**MIC breakpoint (mg/L)**		**Disk content (µg)**	**Zone diameter breakpoint (mm)**	
	S ≤	**R >**		**S ≥**	**R <**
Linezolid	4	4	10	21[A]	21[A]
Tedizolid	0.5[1]	0.5		Note[B]	Note[B]

Staphylococcus

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

Cephalosporins[1]	MIC breakpoint (mg/L)		Disk content (µg)
	S ≤	R >	
Cefaclor[2]	Note[1]	Note[1]	
Cefadroxil	Note[1]	Note[1]	
Cefalexin	Note[1]	Note[1]	
Cefazolin	Note[1]	Note[1]	
Cefepime	Note[1]	Note[1]	
Cefixime	-	-	
Cefotaxime	Note[1]	Note[1]	
Cefoxitin (screen), *S. aureus* and coagulase-negative staphylococci other than *S. epidermidis*	Note[3,4]	Note[3,4]	30
Cefoxitin (screen), *S. epidermidis*	Note[4]	Note[4]	30
Ceftazidime	-	-	
Ceftazidime-avibactam	-	-	
Ceftibuten	-	-	
Ceftobiprole, *S. aureus*	2[6]	2[6]	5
Ceftolozane-tazobactam	-	-	

Addendum (July 2017) to EUCAST breakpoint t

Breakpoints to be included in EUCAST breakpoint tables v 8.0, January 2018

The European Medicines Agency in May 2017 approved a higher dosing ceftaroline. This has led to EUCAST introducing an intermediate categor corresponding change in the disk diffusion breakpoints

Organisms	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Staphylococcus aureus[1]	1[2]	2[2]	**5**	20	17

2. The S-breakpoint is based on standard dosage (0.6 g x 2 iv over 1 hour) and the I-breakpoint on high dosage (0.6 g x 3 over 2 hours). In pneumonia, there is no clinical data on the treatment of *S. aureus* with MICs above 1 mg/L.
There is some PK-PD evidence to suggest that treatment of complicated skin and skin structure infections caused by *S. aureus* with MICs of 4 mg/L could be possible with the regimen of 600 mg every 8 hours using a two-hour infusion. Isolates with MICs above 2 mg/L are rare.

Pseudomonas s

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

Cephalosporins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	-	-		-	-
Cefadroxil	-	-		-	-
Cefalexin	-	-		-	-
Cefazolin	-	-		-	-
Cefepime[1]	8	8	30	19	19
Cefixime	-	-		-	-
Cefotaxime	-	-		-	-
Cefoxitin	NA	NA		NA	NA
Cefpodoxime	-	-		-	-
Ceftaroline	-	-		-	-
Ceftazidime[2]	8	8	10	17	17
Ceftazidime-avibactam, *P. aeruginosa*	8[3]	8[3]	10-4	17	17
Ceftibuten	-	-		-	-
Ceftobiprole	IE	IE		IE	IE
Ceftolozane-tazobactam, *P. aeruginosa*	4[4]	4[4]	30-10	IP	IP
Ceftriaxone	-	-		-	-
Cefuroxime iv	-	-		-	-
Cefuroxime oral	-	-		-	-

Addendum (June 2017) to the EUCAST breakpoint table v. 7.1

Breakpoints to be included in EUCAST breakpoint tables v 8.0, January 2018

For ceftolozane-tazobactam zone diameter breakpoints for *Pseudomonas aeruginosa* are lacking in the current EUCAST breakpoint table. EUCAST has decided to publish the zone diameter breakpoints now instead of delaying publication until January 2018.

***Pseudomonas aeruginosa* and ceftolozane-tazobactam**	**MIC breakpoint (mg/L)**		**Disk content (µg)**	**Zone diameter breakpoint (mm)**	
	S ≤	**R >**		**S ≥**	**R <**
EUCAST Breakpoint Table v 7.1	4[1]	4[1]		IP	IP
Revised breakpoints 2017	4[1]	4[1]	**30-10**	24	24

1. For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.
IP = In Preparation

Changes from EUCAST Breakpoint Tables v 7.1 is highlighted in yellow.

Rimini, 13 novembre 2017

Enterobacteriaceae

EUCAST Clinical Breakpoint Tables v. 7.1, valid from 2017-03-10

Cephalosporins[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	-	-		-	-
Cefadroxil (uncomplicated UTI only)	16	16	30	12	12
Cefalexin (uncomplicated UTI only)	16	16	30	14	14
Cefazolin	-	-		-	-
Cefepime	1	4	30	27	21
Cefixime (uncomplicated UTI only)	1	1	5	17	17
Cefotaxime	1	2	5	20	17
Cefoxitin (screen)[2]	NA	NA	30	19	19
Cefpodoxime (uncomplicated UTI only)	1	1	10	21	21
Ceftaroline	0.5	0.5	5	23	23
Ceftazidime	1	4	10	22	19
Ceftazidime-avibactam	8[3]	8[3]	10-4	13	13
Ceftibuten (UTI only)	1	1	30	23	23
Ceftobiprole	0.25	0.25	5	23	23
Ceftolozane-tazobactam	1[4]	1[4]	30-10	23	23
Ceftriaxone	1	2	30	25	22
Cefuroxime iv[5], *E. coli, Klebsiella* spp. and *P. mirabilis*	8	8	30	19	19
Cefuroxime oral (uncomplicated UTI only)	8	8	30	19	19

Streptococcus pneumoniae

EUCAST Clinical Breakpoint Tables v. 7.1, valid from 2017-03-10

Cephalosporins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	0.03	0.5	30	50	28
Cefadroxil	-	-		-	-
Cefalexin	-	-		-	-
Cefazolin	-	-		-	-
Cefepime	1	2		Note[A]	Note[A]
Cefixime	-	-		-	-
Cefotaxime	0.5	2		Note[A]	Note[A]
Cefoxitin	NA	NA		NA	NA
Cefpodoxime	0.25	0.5		Note[A]	Note[A]
Ceftaroline	0.25	0.25		Note[A]	Note[A]
Ceftazidime	-	-		-	-
Ceftazidime-avibactam	-	-		-	-
Ceftibuten	-	-		-	-
Ceftobiprole	0.5	0.5		Note[A]	Note[A]
Ceftolozane-tazobactam	-	-		-	-
Ceftriaxone	0.5	2		Note[A]	Note[A]

Acinetobacter s

EUCAST Clinical Breakpoint Tables v. 7.1, valid fron

Cephalosporins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	-	-		-	-
Cefadroxil	-	-		-	-
Cefalexin	-	-		-	-
Cefazolin	-	-		-	-
Cefepime	-	-		-	-
Cefixime	-	-		-	-
Cefotaxime	-	-		-	-
Cefoxitin	-	-		-	-
Cefpodoxime	-	-		-	-
Ceftaroline	-	-		-	-
Ceftazidime	-	-		-	-
Ceftazidime-avibactam	-	-		-	-
Ceftibuten	-	-		-	-
Ceftobiprole	-	-		-	-
Ceftolozane-tazobactam	-	-		-	-
Ceftriaxone	-	-		-	-
Cefuroxime iv	-	-		-	-

Enterococcus spp.

EUCAST Clinical Breakpoint Tables v. 7.1, valid from 2017-03-10

Cephalosporins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Cefaclor	-	-		-	-
Cefadroxil	-	-		-	-
Cefalexin	-	-		-	-
Cefazolin	-	-		-	-
Cefepime	-	-		-	-
Cefixime	-	-		-	-
Cefotaxime	-	-		-	-
Cefoxitin	-	-		-	-
Cefpodoxime	-	-		-	-
Ceftaroline	-	-		-	-
Ceftazidime	-	-		-	-
Ceftazidime-avibactam	-	-		-	-
Ceftibuten	-	-		-	-
Ceftobiprole	-	-		-	-
Ceftolozane-tazobactam	-	-		-	-
Ceftriaxone	-	-		-	-

Antibiotic innovation for future public health needs

U. Theuretzbacher*

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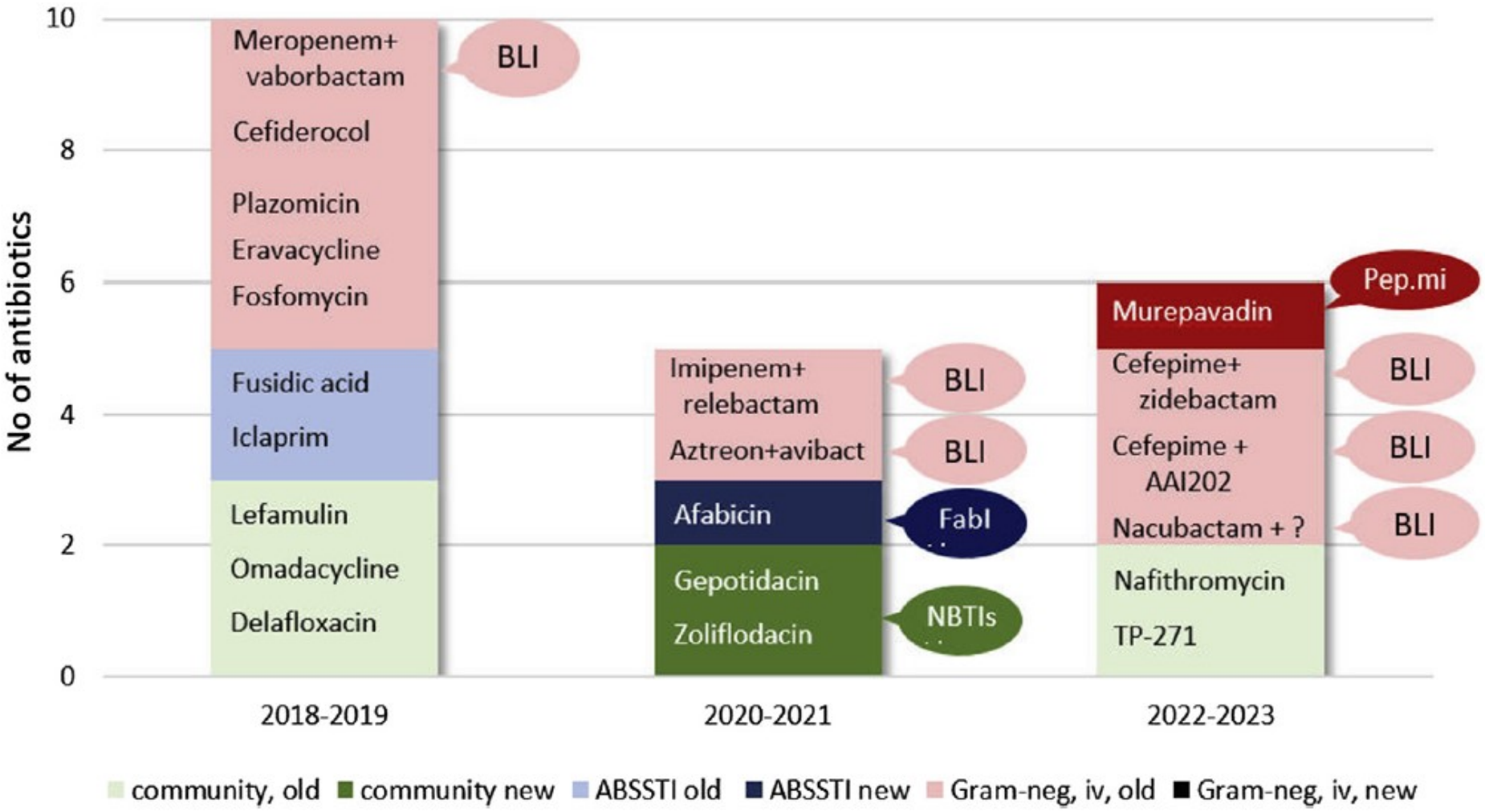

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