

Staphylococcus spp.

EUCAST Clinical Breakpoint Table v. 4.0, valid from 2014-01-01

Disk diffusion (EUCAST standardised disk diffusion method) Medium: Mueller-Hinton agar Inoculum: McFarland 0.5 Incubation: Air, 35±1°C, 18±2h Reading: Read zone edges as the point showing no growth viewed from the back of the plate against a dark background illuminated with reflected light. Quality control: <i>Staphylococcus aureus</i> ATCC 29213

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 <	
						1/A. With the exception of <i>S. saprophyticus</i> , most staphylococci are penicillinase producers. The benzylpenicillin breakpoint will mostly, but not unequivocally, separate beta-lactamase producers from non-producers. If the MIC is >0.12 mg/L, report resistant. If the MIC is ≤0.12mg/L, test susceptibility with the benzylpenicillin disk (see note B). Isolates positive for beta-lactamase are resistant to benzylpenicillin, phenoxymethylpenicillin, amino-, carboxy- and ureidopenicillins. Isolates negative for beta-lactamase and susceptible to cefoxitin (cefoxitin is used to screen for "methicillin resistance") can be reported susceptible to these drugs. Isolates positive for beta-lactamase and susceptible to cefoxitin are susceptible to penicillin-beta-lactamase inhibitor combinations and penicillinase-resistant penicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin). Isolates resistant to cefoxitin are methicillin resistant and resistant to beta-lactam agents, except those with approved anti-MRSA activity and clinical breakpoints.
Benzylpenicillin, <i>S. aureus</i>	0.12 ¹	0.12 ^{1,2}	1 unit	26 ^{A,B}	26 ^{A,B}	B. Disk diffusion is more reliable than MIC for detection of penicillinase producers, provided the zone diameter is measured AND the zone edge closely inspected (see pictures below). If the zone diameter is <26 mm, report resistant. If the zone diameter is ≥26 mm AND the zone edge is sharp, report resistant. If not sharp, report susceptible and if uncertain, report resistant. Chromogenic cephalosporin-based beta-lactamase tests do not reliably detect staphylococcal penicillinase.
Benzylpenicillin, Coagulase negative staphylococci	IE	IE	1 unit	Note ^C	Note ^C	C. Coagulase negative staphylococci are mostly resistant to benzylpenicillin due to penicillinase production, methicillin resistance or both. To report an isolate susceptible to benzylpenicillin, the zone diameter must be ≥ 26 mm, methicillin resistance must be excluded and penicillinase production must be excluded by a PCR test for <i>blaZ</i> . (PCR for <i>blaZ</i> is not definitive for all CNS)
Ampicillin, <i>S. saprophyticus</i>	Note ¹	Note ¹	2	18 ^{A,D}	18 ^{A,D}	D. Ampicillin susceptible <i>S. saprophyticus</i> are methicillin susceptible and there is no need to screen for methicillin resistance with cefoxitin.
Ampicillin-sulbactam	Note ¹	Note ¹		Note ^A	Note ^A	Note E?
Amoxicillin	Note ¹	Note ¹		Note ^A	Note ^A	Note E?
Amoxicillin-clavulanate	Note ¹	Note ¹		Note ^A	Note ^A	Note E?
Piperacillin	Note ¹	Note ¹		Note ^A	Note ^A	Note E?
Piperacillin-tazobactam	Note ¹	Note ¹		Note ^A	Note ^A	Note E?
Ticarcillin	Note ¹	Note ¹		Note ^A	Note ^A	
Ticarcillin-clavulanate	Note ¹	Note ¹		Note ^A	Note ^A	
Phenoxymethylpenicillin	Note ¹	Note ¹		Note ^A	Note ^A	
Oxacillin ²	Note ^{1,2}	Note ^{1,2}		Note ^A	Note ^A	2. <i>S. aureus</i> and <i>S. lugdunensis</i> with oxacillin MIC values >2 mg/L are mostly methicillin resistant due to the presence of the <i>mecA</i> gene. The corresponding oxacillin MIC for coagulase-negative staphylococci is >0.25 mg/L.
Cloxacillin	Note ¹	Note ¹		Note ^A	Note ^A	
Dicloxacillin	Note ¹	Note ¹		Note ^A	Note ^A	
Flucloxacillin	Note ¹	Note ¹		Note ^A	Note ^A	

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Mecillinam (uncomplicated UTI only)	-	-		-	-	
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Cephalosporins 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. Susceptibility of staphylococci to cephalosporins is inferred from the ceftazidime, ceftazidime, cefixime and ceftibuten, which do not have breakpoints and should not be used for staphylococcal infections. Some methicillin-resistant <i>S. aureus</i> are susceptible to ceftaroline, see Note 5/B .
Cefaclor ²	Note ¹	Note ¹		Note ^A	Note ^A	2. High-dose therapy is required for treatment of staphylococcal infections. A. Susceptibility inferred from ceftazidime.
Cefadroxil	Note ¹	Note ¹		Note ^A	Note ^A	
Cefalexin	Note ¹	Note ¹		Note ^A	Note ^A	
Cefazolin	Note ¹	Note ¹		Note ^A	Note ^A	
Cefepime	Note ¹	Note ¹		Note ^A	Note ^A	
Cefixime	-	-		-	-	
Cefotaxime	Note ¹	Note ¹		Note ^A	Note ^A	
Cefoxitin (screen), <i>S. aureus</i> , <i>S. lugdunensis</i> and <i>S. saprophyticus</i>	Note ³	Note ³	30	22 ^A	22 ^A	3. <i>S. aureus</i> and <i>S. lugdunensis</i> with ceftazidime MIC values >4 mg/L are methicillin resistant, mostly due to the presence of the <i>mecA</i> gene. Disk diffusion reliably predicts methicillin resistance.
Cefoxitin (screen), Coagulase negative staphylococci other than <i>S. lugdunensis</i> and <i>S. saprophyticus</i>	Note ⁴	Note ⁴	30	25 ^{A,B}	25 ^{A,B}	4. For coagulase-negative staphylococci other than <i>S. lugdunensis</i> the ceftazidime MIC is a poorer predictor of methicillin resistance than the disk diffusion test. B. Good growth is essential for a reliable screening test.
Cefoxitin (screen), <i>S. pseudintermedius</i>	Note ⁴	Note ⁴	30	35 ^{A,B}	35 ^{A,B}	
Cefpodoxime	Note ¹	Note ¹		Note ^A	Note ^A	
Ceftaroline, <i>S. aureus</i>	1 ⁵	1 ⁵	5	20 ^C	20 ^C	5/C. Methicillin-susceptible isolates can be reported susceptible to ceftaroline without further testing. The ceftaroline zone diameter breakpoints are set to avoid reporting resistant isolates as susceptible. For methicillin-resistant isolates with ceftaroline zone diameters 18-20 mm, an MIC can be performed to confirm the disk diffusion test result.
Ceftazidime	-	-		-	-	
Ceftibuten	-	-		-	-	
Ceftriaxone	Note ¹	Note ¹		Note ^A	Note ^A	
Cefuroxime iv	Note ¹	Note ¹		Note ^A	Note ^A	
Cefuroxime oral	Note ¹	Note ¹		Note ^A	Note ^A	

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/A. Susceptibility of staphylococci to carbapenems is inferred from the ceftazidime susceptibility.
Doripenem	Note ¹	Note ¹		Note ^A	Note ^A	
Ertapenem	Note ¹	Note ¹		Note ^A	Note ^A	
Imipenem	Note ¹	Note ¹		Note ^A	Note ^A	
Meropenem	Note ¹	Note ¹		Note ^A	Note ^A	

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Monobactams	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 <	
Aztreonam	-	-		-	-	

Fluoroquinolones 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. For breakpoints for other fluoroquinolones (e.g. pefloxacin and enoxacin), refer to breakpoints set by national breakpoint committees.
Ciprofloxacin ²	1	1	5	20 ^A	20 ^A	2. Breakpoints relate to high dose therapy. A. The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. See Note B.
Levofloxacin	1	2	5	22 ^A	19 ^A	
Moxifloxacin	0.5	1	5	24 ^A	21 ^A	
Nalidixic acid (screen)	NA	NA		NA	NA	
Norfloxacin (screen)	NA	NA	10	17 ^B	Note ^B	B. Isolates categorised as susceptible to norfloxacin can be reported susceptible to ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.
Ofloxacin ²	1	1	5	20 ^A	20 ^A	

Aminoglycosides 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. Aminoglycoside breakpoints are based on once-daily administration of high aminoglycoside dosages. Most often aminoglycosides are given in combination with beta-lactam agents.
Amikacin ² , <i>S. aureus</i>	8	16	30	18	16	2. Resistance to amikacin is most reliably determined by testing with kanamycin (zone diameter breakpoints under development).
Amikacin ² , Coagulase-negative staphylococci	8	16	30	22	19	
Gentamicin, <i>S. aureus</i>	1	1	10	18	18	
Gentamicin, Coagulase-negative staphylococci	1	1	10	22	22	
Netilmicin, <i>S. aureus</i>	1	1	10	18	18	
Netilmicin, Coagulase-negative staphylococci	1	1	10	22	22	
Tobramycin, <i>S. aureus</i>	1	1	10	18	18	
Tobramycin, Coagulase-negative staphylococci	1	1	10	22	22	

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Glycopeptides 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. Glycopeptide MICs are method dependent and should be determined by broth microdilution (reference ISO 20776). <i>S. aureus</i> with vancomycin MIC values of 2 mg/L are on the border of the wild type MIC distribution and there may be an impaired clinical response. The resistant breakpoint has been reduced to 2 mg/L to avoid reporting "GISA" isolates intermediate as serious infections with "GISA" isolates are not treatable with increased doses of vancomycin or teicoplanin.
Teicoplanin, <i>S. aureus</i>	2	2		Note ^A	Note ^A	A. Disk diffusion is unreliable and cannot distinguish between wild type isolates and those with non- <i>vanA</i> -mediated resistance.
Teicoplanin, Coagulase-negative staphylococci	4	4		Note ^A	Note ^A	
Telavancin, MRSA	1	1		Note ^A	Note ^A	
Vancomycin, <i>S. aureus</i>	2	2		Note ^A	Note ^A	
Vancomycin, Coagulase-negative staphylococci	4	4		Note ^A	Note ^A	

Macrolides, lincosamides and streptogramins	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 <	
Azithromycin	1 ¹	2 ¹		Note ^A	Note ^A	1/A. Erythromycin can be used to determine susceptibility to azithromycin, clarithromycin and roxithromycin.
Clarithromycin	1 ¹	2 ¹		Note ^A	Note ^A	
Erythromycin	1 ¹	2 ¹	15	21 ^A	18 ^A	
Roxithromycin	1 ¹	2 ¹		Note ^A	Note ^A	
Telithromycin	IE	IE		IE	IE	
Clindamycin ²	0.25	0.5	2	22 ^B	19 ^B	2/B. Inducible clindamycin resistance can be detected only in the presence of a macrolide antibiotic. In disk diffusion tests look for apparent antagonism of clindamycin by erythromycin (D-test).
Quinupristin-dalfopristin	1	2	15	21 ^C	18 ^C	C. Isolates non-susceptible by disk diffusion should be confirmed by MIC testing.

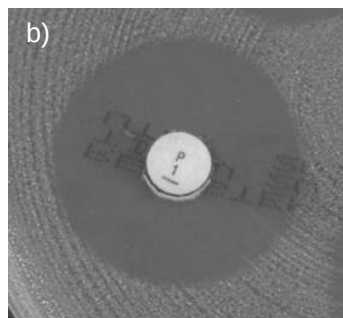
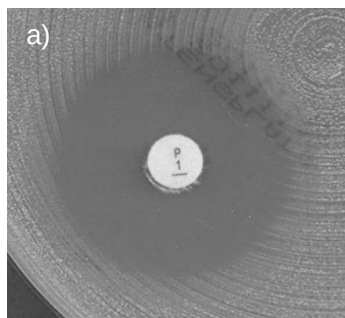
Tetracyclines	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R >		S ≥	R <	
Doxycycline	1 ¹	2 ¹		Note ^A	Note ^A	1/A. Isolates susceptible to tetracycline are also susceptible to doxycycline and minocycline, but some resistant to tetracycline may be susceptible to minocycline and/or doxycycline. An MIC method should be used to test doxycycline susceptibility of tetracycline resistant isolates if required.
Minocycline	0.5 ¹	1 ¹	30	23 ^A	20 ^A	
Tetracycline	1 ¹	2 ¹	30	22 ^A	19 ^A	

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Tigecycline	0.5 ²	0.5	15	18	18	2. Isolates with MIC values above the susceptible breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC values above the current resistant breakpoint they should be reported resistant.
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Miscellaneous	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 <	
Chloramphenicol	8	8	30	18	18	
Colistin	-	-		-	-	
Daptomycin	1	1 ¹		Note ^A	Note ^A	1. Isolates with MIC values above the susceptible breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC values above the current resistant breakpoint they should be reported resistant. A. Use an MIC method.
Fosfomycin iv	32	32		Note ^A	Note ^A	
Fosfomycin oral	-	-		-	-	
Fusidic acid	1	1	10	24	24	
Linezolid	4	4	10	19 ^B	19 ^B	B. Examine zone edges with transmitted light (plate held up to light).
Metronidazole	-	-		-	-	
Mupirocin	1 ²	256 ²	200	30 ^C	18 ^C	2/C. Breakpoints relate to nasal decolonisation of <i>S. aureus</i> . Intermediate isolates are initially cleared as effectively as susceptible isolates but recolonisation is very common.
Nitrofurantoin (uncomplicated UTI only)	64 ³	64 ³	100	13 ^C	13 ^C	3/C. Breakpoints apply to <i>S. saprophyticus</i> only.
Rifampicin	0.06	0.5	5	26	23	
Spectinomycin	-	-		-	-	
Trimethoprim (uncomplicated UTI only)	2	4	5	17	14	
Trimethoprim-sulfamethoxazole ⁴	2	4	1.25-23.75	17	14	4. Trimethoprim:sulfamethoxazole in the ratio 1:19. Breakpoints are expressed as the trimethoprim concentration.



Examples of inhibition zones for *Staphylococcus aureus* with benzylpenicillin.

- a) Fuzzy zone edge and zone diameter ≥ 26 mm. Report susceptible.
b) Sharp zone edge and zone diameter ≥ 26 mm. Report resistant.

We do not think *S.lugdunensis* should be added to the *S.aureus* comment. **See presentation on staphylococci and penicillinase.**

S. lugdunensis : We are waiting for Sören's data. In Växjö all 20 blaZ positive strains exhibited zone diameters <20 mm and all 30 blaZ-negative isolates zone diameters <24 mm. The correlation between blaZ status and zone edge was not sufficiently good. **See presentation on staphylococci and penicillinase.**

See presentation on minor breakpoint adjustments

E. Susceptibility to ampicillin, amoxicillin and piperacillin with and without beta-lactamase inhibitor can be inferred from ampicillin. **Don't think that works as ampicillin is only for saprophyticus**

Note B added

Comment reworded as discussed on the September meeting.

A presentation on the Scandinavian multi-laboratory study will be available before the meeting.

Recommendation on interpretation?

Should the distance between the disks be stated only in the manual or in the bp table as well?

Pictures will be added to **the reading guide**.

See separate presentation on inducible clindamycin resistance (will be available before the meeting).

