Resistance Surveillance Programme Report for European Nations (2011)

P1503

RN JONES, HS SADER, RK FLAMM, JM STREIT, RM MENDES, M CASTANHEIRA

JMI Laboratories, North Liberty, Iowa, USA

ECCMID 2013
JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
319.665.3370, fax 319.665.3371
ronald-jones@jmilabs.com

AMENDED ABSTRACT

Background: In the European (EU) component of an Emerging Markets (EM) resistance (R) surveillance study **(**EMRS; 2011), 21 countries overall were monitored for antimicrobial R patterns including Belgium, Bulgaria (BU), Croatia (CR), Czech Republic (CZ), France (F), Germany, Greece (GR), Ireland, Israel (IS), Italy (IT), Poland (PO), Portugal, Romania (RO), Russia, Slovakia (SK), Slovenia, Spain, Sweden, Turkey (T), Ukraine and United Kingdom (UK).

Methods: Results from testing 12,572 strains (100 [BU] to 1535 [F] per nation) were interpreted by CLSI, EUCAST and USA-FDA breakpoints. Samples from 47 sites were reference tested versus potent, marketed agents: linezolid (LZD), vancomycin (VAN), tigecycline (TIG), colistin (COL), cefoperazone/sulbactam (C/S), amikacin (AMK), levofloxacin (LEV) and 21 others. R mechanisms were screened by PCR.

Results: Among *S. aureus* (SA; **Table**), LZD (MIC_{90}, 1 mg/L), TIG (MIC_{90}, 0.12 mg/L) and VAN (MIC_{90}, 1 mg/L) exhibited complete coverage and MRSA rates among EM nations ranged from 16% (BU) to 60% (PO, RO, SK). LZD-R-CoNS (7) were noted in 4 western EU nations and in a *S. simulans* strain (MIC, 8 mg/L) from RO having L3 mutations (N130D, G152A, F147S, A157R); also 4 LZD-R enterococci. VRE (84% VanA) were noted in CZ (13%), IS (4%), RO (5%) and T (20%). ESBL rate for *E. coli* was 20% (range, 10% [CR, SK] to 70% [BU], best inhibited by COL (100%S), TIG (100%), AMK (83%), C/S (88%) and carbapenems (99%; R strains in IS & T). *Klebsiella* spp. had greater ESBL rates (46% overall, range 31-100%) as well as carbapenem-R (8% overall, greatest in BU, GR, IS, IT, PO, RO). Nonfermentors (*P. aeruginosa*, *Acinetobacter* [ACB]) were generally very R except against COL (99% S) and TIG (95% S at ≤2 mg/L; ACB only). The following carbapenemases were noted: VIM-1 (2 countries); IMP-1 (1 from T); KPC-2 or -3 (2 countries); VIM-4 (1 from PO), NDM-1 (2 in RO; 2 centres); and OXA-48 or -162 (5 from T; 2 centres).

Conclusions: EU surveillance sampling demonstrates a wide array of R isolates, less prevalent among Gram-positives that remain inhibited by available agents (LZD, TIG, VAN). However, beta-lactamase-mediated-R has spread widely among Gram-negatives, especially across the eastern EU and EM nations, severely limiting infection chemotherapy.

Antimicrobials	EU S rates (EUCAST criteria) for key Gram-positive pathogens (no.):[a] SA (2413)	CoNS (622)	ENT (555)	SPN (631)	BHS (410)
Oxacillin[b]	69	26	64	69	100
LZD	100	99[c]	99[d]	100	100
TIG	100	100	100	100	100
VAN	100	99	90	100	100
Macrolides[e]	67	35	-	69	78
LEV	71	46	-	-	95
TMP/SMX	99	62	48	72	98
Ceftriaxone	69	26	-	81	100

a. ENT=enterococci; SPN=*S. pneumoniae*; BHS=β-haemolytic streptococci. b. Ampicillin for ENT and penicillin for the streptococci c. R strains from F, GR, IT, RO and Spain. d. R strains from Germany, Ireland and T. e. S rates for erythromycin-like agents.

INTRODUCTION

Bacterial strains resistant to commonly used β-lactams, fluoroquinolones and other antimicrobial agents remain a significant challenge to successful chemotherapy in both developed and developing nations. β-lactamase-mediated resistances among Gram-negative bacilli and the expansion of Gram-positive resistant species (methicillin-resistant *Staphylococcus aureus* [MRSA], vancomycin-resistant enterococci [VRE], multidrug-resistant [MDR] *Streptococcus pneumoniae*) present the most critical compromise to favorable patient outcomes.

To address these concerns, a structured antimicrobial surveillance program was organized for 2011 to 1.) sample key pathogens by nation in the European area; 2.) use reference quantitative susceptibility testing methods (Clinical and Laboratory Standards Institute [CLSI]) in regulated central monitoring laboratories; and 3.) offer a wide range of tested antimicrobials, usually 20-40 agents. These program results then can be compared to other regional or national surveillance programs that utilize available "non-reference" (convenience samples), often commercial categorical (not quantitative) results. The categorical susceptible breakpoint definitions may vary as well as the quality/accuracy of the method; therefore structured programs such as this Emerging Markets Resistance Surveillance (EMRS) Programme offers expanded, validating information for other programmes, especially for eastern Europe and Mediterranean.

In the European component of EMRS, 21 nations were monitored in 2011 (12,572 isolates), enabling comparison of more than 30 drugs to that data generated by the EARS-Net and other published programme information.

METHODS

Nations and organisms monitored. A total of 21 countries (47 sites, 97-492 strains/site) were sampled with a target of ≥200 isolates of specific species per nation. The organisms were isolated from a wide variety of clinical infection types/sites including respiratory tract (26.3%), acute bacterial skin and skin structure (17.2%), and bacteremias (26.3%). The countries (sample size) were: Belgium (492), Bulgaria (100), Croatia (200), Czech Republic (447), France (1,535), Germany (756), Greece (418), Ireland (722), Israel (225), Italy (1,110), Poland (505), Portugal (441), Romania (367), Russia (588), Slovakia (200), Slovenia (252), Spain (1,066), Sweden (540), Turkey (1,198), Ukraine (244), and United Kingdom (UK; 750). The organisms directed to be sampled included: *S. aureus* (2,413), coagulase-negative staphylococci (CoNS; 622), enterococci (555), *S. pneumoniae* (631), viridans and β-haemolytic streptococci (654), *E. coli* (2,115), *Klebsiella* spp. (1,076), *Enterobacter* spp. (578), other Enterobacteriaceae (four species groups [**Table 2**]), *P. aeruginosa* (1,185) and *Acinetobacter* spp. (472). Organisms detected with resistance to key, marketed agents were tested by various molecular methods such as PCR amplification/ sequencing, example extended spectrum β-lactamases (ESBLs), metallo-β-lactamases (MBLs), MDR Gram-negative bacilli or Gram-positive cocci.

Methods and antimicrobials tested. CLSI M07-A9 (2012) methods were applied using validated broth microdilution panels produced by ThermoFisher Scientific Inc., formerly TREK Diagnostics (Cleveland, Ohio, USA). Interpretations of results utilized CLSI (M100-S23, 2013), USA-Food and Drug Administration (FDA) and EUCAST (2013) criteria; and the results of quality control (QC) tests were dominantly (nearly 99.0%) within QC ranges for six utilized control organisms.

The sponsor (Pfizer Inc., New York, New York, USA) -produced compounds included: linezolid, tigecycline, piperacillin/tazobactam, ampicillin/sulbactam, cefoperazone and cefoperazone/sulbactam. For studying Gram-negative bacilli, Gram-positive cocci, and fastidious respiratory tract species numerous additional (15-20) drugs were also tested.

ESBL patterns were defined for *E. coli*, *Klebsiella* spp. and *P. mirabilis* per CLSI (2013) criteria as a MIC of ≥2 mg/L for aztreonam or ceftriaxone or ceftazidime. Carbapenem-resistant Enterobacteriaceae (CRE) were noted by a MIC at ≥2 mg/L for doripenem or imipenem or meropenem.

RESULTS

Antimicrobial profiles of Gram-positive pathogens (**Table 1**)

- *S. aureus* isolates (2,413; 31.3% MRSA overall) exhibited complete (100.0%) susceptibility to linezolid ($MIC_{50/90}$, 1/2 mg/L), teicoplanin ($MIC_{50/90}$, ≤2/≤2 mg/L), tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L) and vancomycin ($MIC_{50/90}$, 1/1 mg/L). Rare resistances to daptomycin (0.1%; strains from Croatia, Germany, Greece and Turkey), doxycycline (4.1-8.8%) and TMP/SMX (1.1%) were observed.
- CoNS samples (622; 74.0% methicillin-resistant) showed common co-resistances and only five agents with >90% susceptibility including linezolid, daptomycin, doxycycline, teicoplanin and vancomycin (94.4 to 100.0% susceptible). The rare occurrences of linezolid non-susceptibility (1.1%) occurred in France (1), Greece (2), Italy (2), Romania (1) and Spain (1). Four *S. epidermidis* strains had *cfr*-mediated resistance (MICs, 4->128 mg/L).
- Enterococci (555; 96.6% either *E. faecalis* or *E. faecium*) had a VRE rate of 10.1%, with 84.2% having a VAN-A pattern. Thirteen nations had VRE (range, 3.1% [Sweden] - 22.6% [Ireland]) and the best agents (% susceptible) were linezolid (99.3), daptomycin (100.0), teicoplanin (91.5) and vancomycin (89.9%). Four linezolid *E. faecium* (Germany [2], Ireland, Turkey) all had G2576 mutations.
- *S. pneumoniae* (631) showed a penicillin-susceptible rate of only 68.6% and ceftriaxone non-susceptible rates varied from 8.1 (CLSI) to 19.2% (EUCAST). Ceftriaxone across 16 nations showed compromised coverage (1.7-44.4% resistance), highest MICs occurring in eastern Europe (Bulgaria, Croatia, Poland, Romania, Turkey and Ukraine). Levofloxacin non-susceptible strains were found in six countries (rates at 2.1-10.0%). Linezolid, tigecycline and vancomycin exhibited 99.8-100.0% susceptibility.

Antimicrobial profiles of Gram-negative bacilli (**Table 2**)

- *E. coli* (2,115) showed β-lactam resistance mechanisms of 20.1% ESBLs (**Table 3**) and only 0.2% CRE. Overall, the most active agents (% susceptible) against *E. coli* were tigecycline (100.0%, EUCAST), meropenem (99.9%), imipenem (99.8%), amikacin (95.7 - 98.6%) and cefoperazone/sulbactam (95.2%). All countries had ESBL phenotype strains (1.0% [Sweden] to 89.7% [Russia], but only two nations had CRE (Israel and Turkey). Highest ESBL rates (>40.0%) occurred in Bulgaria, Poland, Russia, Turkey and Ukraine (**Table 3**).
- *Klebsiella* spp. (1,076) had the highest β-lactam resistance rates with ESBLs at 45.7% (range, 2.5 [Sweden] to 82.4-100.0% [Bulgaria, Poland, Russia and Slovakia]); and CRE was found in 10 countries at 0.9 to 38.8%, highest in Poland and Italy (32.5 - 38.8%), see **Tables 2** and **3**. The best activity versus *Klebsiella* spp. was observed for tigecycline (99.0% susceptible), colistin (96.7, data not shown), meropenem (91.3%) and amikacin (90.9%). **Table 3** shows the compromised coverage of 12 antimicrobials against *Klebsiella* spp. with an ESBL phenotype profile.
- *Enterobacter* spp. (578) and other enteric bacilli showed varying resistance patterns ranging from high rates of susceptibility for *P. mirabilis* and Indole-positive Proteae to high levels of resistance found in some *Citrobacters*, *Enterobacters* and *Serratia* spp. (**Table 2**).

Antimicrobial profiles of *P. aeruginosa* and *Acinetobacter* spp. (**Table 2**)

- *P. aeruginosa* (1,185) strains had more limited susceptibility to many antimicrobials with >90% of samples inhibited only by colistin (99.6% by CLSI and EUCAST criteria). All other tested agents provided a coverage in the 60.0-80.0% range, highest for amikacin (77.5-80.6%) and other aminoglycosides (70.3-71.9%).
- *Acinetobacter* spp. isolates (47.2; 86.0% *A. baumannii*) were generally MDR with only colistin (99.2% susceptible) and tigecycline (MIC_{90}, 2 mg/L) showing activity. All other tested agents (**Table 2**) exhibited <50.0% susceptibility rates.

CONCLUSIONS

- Resistances in Gram-positive pathogens across Europe remains elevated, particularly among *S. aureus* (MRSA) and CoNS, but some agents still have high activity (linezolid, daptomycin and glycopeptides). Enterococcal resistance (VRE at 10.1%) was rare for linezolid and daptomycin, and not increasing. Ceftriaxone non-susceptibility among pneumococci (19.2%) was most worrisome, but linezolid, tigecycline, some fluoroquinolones and vancomycin remain potent options for therapy.
- Enterobacteriaceae shows widespread ESBL and CRE profiles, especially among *Klebsiella* spp. The ESBL/CRE rates in *E. coli* and *Klebsiella* spp. were 20.1/0.2% and 45.7/8.3%, respectively. Resistance rates among enteric bacilli were greatest in southeastern Europe confirming EARRS-Net data. Few agents (amikacin, colistin, some carbapenems, tigecycline) were active against these emerging species.
- *P. aeruginosa* and *A. baumannii* were generally MDR, only having >90.0% susceptibility to polymyxins and tigecycline (*Acinetobacter* spp. only).
- Resistance rates in Europe for 2011 indicate escalating prevalence and needs for combination empiric treatment regimens, as well as development of new agents/enzyme-inhibitor combinations. Surveillance programmes should be supported to monitor emerging trends in resistance and the impact of regional interventions.

ACKNOWLEDGMENTS

The co-authors wish to thank the participants/sites for contributing the isolates and especially Alexander University Hospital, Sofia, Bulgaria (Dr. B. Markova); Clinical Hospital Center, Zagreb, Croatia (Dr. V. Plecko); University Hospital, Brno, Czech Republic (Dr. M. Hanslianova); Meir Medical Center, Kfar Saba, Israel (Dr. Y. Paitan); Rambam Medical Center, Haifa, Israel (Dr. H. Sprecher); University Hospital in Krakow, Krakow, Poland (Dr. J. Kedzierska); Medical University Krakow, Krakow, Poland (Dr. M. Bulanda); Clinical Emergency Hospital Floreasca, Bucharest, Romania (Dr. M. Ariciuc); Infectious Disease Hospital, Cluj-Napoca, Romania (Dr. M. Flonta); University Hospital, Nitra, Slovakia (Dr. A. Liskova); Uludag University Medical Faculty, Bursa, Turkey (Dr. C. Ozakin); Cukurova University, Adana, Turkey (Dr. A. Yamen); and Istanbul Medical Faculty, Istanbul, Turkey (Dr. N. Gurler).

This study at JMI Laboratories was supported by an Education/Research grant from Pfizer, Inc (New York, NY), and JMI Laboratories received compensation fees for services in relation to preparing the abstract/poster, which was funded by Pfizer, Inc.

REFERENCES

1. Castanheira M, Mendes RE, Woosley LN, Jones RN (2011). Trends in carbapenemase-producing *Escherichia coli* and *Klebsiella* spp. from Europe and the Americas: Report from the SENTRY Antimicrobial Surveillance Programme (2007-09). *J Antimicrob Chemother* 66: 1409-1411.
2. Clinical and Laboratory Standards Institute (2012). *M07-A9. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard: ninth edition*. Wayne, PA: CLSI.
3. Clinical and Laboratory Standards Institute (2013). *M100-S23. Performance standards for antimicrobial susceptibility testing: 23rd informational supplement.* Wayne, PA: CLSI.
4. European Committee on Antimicrobial Susceptibility Testing (2013). Breakpoint tables for interpretation of MICs and zone diameters. Version 3.0, January 2013. Available at: http://www.eucast.org/clinical_breakpoints/. Accessed January 1, 2013.
5. Flamm RK, Mendes RE, Ross JE, Sader HS, Jones RN (2013). An international activity and spectrum analysis of linezolid: ZAAPS program results for 2011. *Diagn Microbiol Infect Dis in press*.
6. Mendes RE, Deshpande LM, Farrell DJ, Spanu T, Fadda G, Jones RN (2010). Assessment of linezolid resistance mechanisms among *Staphylococcus epidermidis* causing bacteraemia in Rome, Italy. *J Antimicrob Chemother* 65: 2329-2335.
7. Rodloff AC, Leclercq R, Debbia EA, Canton R, Oppenheim BA, Dowzicky MJ (2008). Comparative analysis of antimicrobial susceptibility among organisms from France, Germany, Italy, Spain and the UK as part of the tigecycline evaluation and surveillance trial. *Clin Microbiol Infect* 14: 307-314.
8. Sader HS, Farrell DJ, Jones RN (2011). Antimicrobial activity of daptomycin tested against gram-positive strains collected in European hospitals: results from 7 years of resistance surveillance (2003-2009). *J Chemother* 23: 200-206.
9. Tygacil® Package Insert (2012). Available at www.tygacil.com. Accessed January 2013.

Table 1. Activity of selected antimicrobial agents when tested against 4,875 Gram-positive pathogens from European nations in 2011.

Organism (no. tested) / Antimicrobial agent	MIC (mg/L) 50%	90%	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
S. aureus (2,413)					
Linezolid	1	2	0.25 – 2	100.0 / 0.0	100.0 / 0.0
Tigecycline[b]	0.06	0.12	≤0.03 – 0.5	100.0 / -	100.0 / 0.0
Pip/taz	2	>64	≤0.5 – >64	68.7 / 31.3	68.7 / 31.3
Amox/clav	≤1	>8	≤1 – >8	68.7 / 31.3	68.7 / 31.3
Ceftriaxone	4	>8	0.5 – >8	68.7 / 31.3	68.7 / 31.3
Clindamycin	≤0.25	>2	≤0.25 – >2	87.8 / 12.1	87.4 / 12.2
Daptomycin	0.25	0.5	≤0.06 – 2	99.9 / -	99.9 / 0.1
Doxycycline	0.12	1	≤0.06 – >8	95.9 / 0.7	91.2 / 5.7
Erythromycin	0.25	>16	≤0.12 – >16	67.1 / 30.5	67.4 / 31.8
Gentamicin	≤1	>8	≤1 – >8	89.6 / 10.2	89.2 / 10.8
Levofloxacin	0.25	>4	≤0.12 – >4	70.8 / 28.1	70.8 / 28.1
Meropenem	0.12	>8	≤0.06 – >8	68.7 / 31.3	68.7 / 31.3
Oxacillin	0.5	>2	≤0.25 – >2	68.7 / 31.3	68.7 / 31.3
Penicillin	8	>8	≤0.06 – >8	15.6 / 84.4	15.6 / 84.4
TMP/SMX	≤0.5	≤0.5	≤0.5 – >4	98.9 / 1.1	98.9 / 0.9
Vancomycin	1	1	0.25 – 2	100.0 / 0.0	100.0 / 0.0
CoNS (622)[c]					
Linezolid	0.5	1	≤0.12 – >8	98.9 / 1.1	98.9 / 1.1
Tigecycline[b]	0.06	0.12	≤0.03 – 0.5	- / -	100.0 / 0.0
Pip/taz	2	64	≤0.5 – >64	26.0 / 74.0	26.0 / 74.0
Amox/clav	2	>8	≤1 – >8	26.0 / 74.0	26.0 / 74.0
Ceftriaxone	>8	>8	≤0.06 – >8	26.0 / 74.0	26.0 / 74.0
Clindamycin	≤0.25	>2	≤0.25 – >2	75.1 / 24.6	72.7 / 24.9
Daptomycin	0.5	0.5	≤0.06 – 2	99.8 / -	99.8 / 0.2
Doxycycline	0.5	2	≤0.06 – >8	94.4 / 1.3	85.5 / 10.0
Erythromycin	>16	>16	≤0.12 – >16	34.7 / 64.1	35.0 / 64.6
Gentamicin	≤1	>8	≤1 – >8	55.8 / 36.5	50.0 / 50.0
Levofloxacin	2	>4	≤0.12 – >4	46.1 / 50.0	46.1 / 50.0
Meropenem	2	>8	≤0.06 – >8	26.0 / 74.0	26.0 / 74.0
Oxacillin	>2	>2	≤0.25 – >2	26.0 / 74.0	26.0 / 74.0
Penicillin	4	>8	≤0.06 – >8	13.9 / 86.1	13.9 / 86.1
TMP/SMX	≤0.5	>4	≤0.5 – >4	61.9 / 38.1	61.9 / 22.3
Vancomycin	2	2	0.25 – 4	100.0 / 0.0	100.0 / 0.0
Enterococcus spp.(555)[d]					
Linezolid	1	2	≤0.12 – >8	99.3 / 0.7	99.3 / 0.7
Tigecycline[b]	≤0.03	0.06	≤0.03 – 0.25	100.0 / -	100.0 / 0.0
Pip/taz	8	>64	≤0.5 – >64	64.3 / -	64.3 / -
Amox/clav	≤1	>8	≤1 – >8	64.3 / -	64.3 / 35.8
Ampicillin	1	>8	≤0.25 – >8	64.3 / 35.7	63.8 / 35.7
Daptomycin	1	2	≤0.06 – 4	100.0 / -	- / -
Doxycycline	4	>8	≤0.06 – >8	51.0 / 14.4	- / -
Erythromycin	>16	>16	≤0.12 – >16	7.7 / 64.0	- / -
Imipenem	2	>8	≤0.12 – >8	- / -	63.4 / 36.0
Levofloxacin	>4	>4	≤0.12 – >4	44.3 / 54.1	- / -
Teicoplanin	≤2	≤2	≤2 – >16	91.5 / 8.3	91.2 / 8.8
Vancomycin	1	8	0.25 – >16	89.9 / 9.2	89.9 / 10.1
S. pneumoniae (631)					
Linezolid	1	1	≤0.12 – 2	100.0 / -	100.0 / 0.0
Tigecycline[b]	≤0.03	0.06	≤0.03 – 0.12	99.8 / -	- / -
Amox/clav	≤1	4	≤1 – >8	87.8 / 7.3	- / -
Ceftriaxone	≤0.06	1	≤0.06 – >8	91.6 / 3.0	80.8 / 3.0
Clindamycin	≤0.25	>2	≤0.25 – >2	78.3 / 21.6	78.4 / 21.6
Erythromycin	≤0.12	>16	≤0.12 – >16	68.6 / 30.7	68.6 / 30.7
Levofloxacin	1	1	≤0.12 – >4	98.7 / 1.0	98.7 / 1.3
Meropenem	≤0.06	0.5	≤0.06 – 1	82.4 / 7.3	100.0 / 0.0
Oxacillin	≤0.25	>2	≤0.25 – >2	- / -	- / -
Penicillin[e]	≤0.06	4	≤0.06 – 8	89.7 / 1.1	- / -
Penicillin[f]	≤0.06	4	≤0.06 – 8	68.6 / 17.6	68.6 / 10.3
Tetracycline	0.5	>8	≤0.25 – >8	73.1 / 26.6	72.4 / 26.9
TMP/SMX	≤0.5	>4	≤0.5 – >4	64.3 / 24.9	71.8 / 24.9
Vancomycin	0.25	0.5	≤0.12 – 1	100.0 / -	100.0 / 0.0
β-haemolytic streptococci (410)[g]					
Linezolid	1	1	0.5 – 2	100.0 / -	100.0 / 0.0
Tigecycline[b]	≤0.03	0.06	≤0.03 – 0.12	100.0 / -	100.0 / 0.0
Pip/taz	≤0.5	≤0.5	≤0.5	- / -	100.0 / 0.0
Amox/clav	≤1	≤1	≤1	- / -	100.0 / 0.0
Ceftriaxone	≤0.06	0.12	≤0.06 – 1	99.8 / -	100.0 / 0.0
Clindamycin	≤0.25	≤0.25	≤0.25 – >2	90.5 / 9.3	90.7 / 9.3
Daptomycin	≤0.06	0.25	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Erythromycin	≤0.12	8	≤0.12 – >16	78.0 / 21.5	78.0 / 21.5
Levofloxacin	0.5	1	0.25 – >4	99.3 / 0.7	95.1 / 0.7
Meropenem	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / -	- / -
Penicillin	≤0.06	≤0.06	≤0.06 – 0.12	100.0 / -	100.0 / 0.0
Tetracycline	4	>8	≤0.25 – >8	49.3 / 48.3	47.3 / 50.7
TMP/SMX	≤0.5	≤0.5	≤0.5 – >4	- / -	97.6 / 2.0
Vancomycin	0.5	0.5	≤0.12 – 1	100.0 / -	100.0 / 0.0
viridans group streptococci (244)[h]					
Linezolid	1	1	≤0.12 – 2	100.0 / -	- / -
Tigecycline[b]	≤0.03	0.06	≤0.03 – 0.25	100.0 / -	- / -
Ceftriaxone	0.25	2	≤0.06 – >8	89.3 / 7.8	81.5 / 18.5
Clindamycin	≤0.25	>2	≤0.25 – >2	82.8 / 17.2	82.8 / 17.2
Daptomycin	0.25	1	≤0.06 – 1	100.0 / -	- / -
Erythromycin	0.5	>16	≤0.12 – >16	48.8 / 50.0	- / -
Levofloxacin	1	2	0.25 – >4	94.3 / 5.3	- / -
Meropenem	≤0.06	1	≤0.06 – >8	88.5 / -	95.5 / 4.5
Penicillin	≤0.06	2	≤0.06 – >8	63.5 / 9.4	71.7 / 9.4
Tetracycline	0.5	>8	≤0.25 – >8	63.9 / 33.2	- / -
Vancomycin	0.5	1	0.25 – 1	100.0 / -	100.0 / 0.0

a. Criteria as published by the CLSI [2013] and EUCAST [2013], β-lactam susceptibility should be directed by the oxacillin test results.
b. USA-FDA breakpoints were applied when available [Tygacil Product Insert, 2012].
c. Includes: *Staphylococcus auricularis* (one strain), *S. capitis* (15 strains), *S. caprae* (one strain), *S. chromogenes* (one strain), *S. cohnii* (three strains), *S. epidermidis* (298 strains), *S. haemolyticus* (47 strains), *S. hominis* (69 strains), *S. intermedius* (one strain), *S. lentus* (three strains), *S. lugdunensis* (22 strains), *S. saprophyticus* (six strains), *S. schleiferi* (two strains), *S. sciuri* (one strain), *S. simulans* (five strains), *S. warneri* (seven strains), *S. xylosus* (one strain), unspeciated *Staphylococcus* (one strain), and unspeciated CoNS (138 strains).
d. Includes: *Enterococcus avium* (four strains), *E. faecalis* (334 strains), *E. faecium* (202 strains), *E. gallinarum* (nine strains), *E. hirae* (three strains), and *E. raffinosus* (three strains).
e. Criteria as published by the CLSI [2013] for 'Penicillin parenteral (non-meningitis)'.
f. Criteria as published by the CLSI [2013] for 'Penicillin (oral penicillin V)'.
g. Includes: *Streptococcus dysgalactiae* (eight strains), Group A *Streptococcus* (180 strains), Group B *Streptococcus* (147 strains), Group C *Streptococcus* (22 strains), Group F *Streptococcus* (one strain), and Group G *Streptococcus* (52 strains).
h. Includes: *Streptococcus anginosus* (17 strains), *S. bovis* (13 strains), *S. constellatus* (six strains), *S. equinus* (one strain), *S. gallolyticus* (five strains), *S. gordonii* (one strain), *S. intermedius* (three strains), *S. milleri* (four strains), *S. mitis* (39 strains), *S. mutans* (two strains), *S. oralis* (11 strains), *S. parasanguinis* (three strains), *S. salivarius* (11 strains), *S. sanguinis* (eight strains), *S. suis* (one strain), *S. vestibularis* (three strains), unspeciated *Streptococcus* (two strains), unspeciated alpha-haemolytic streptococci (four strains), and unspeciated viridans group streptococci (110 strains).
Abbreviations: Pip/taz=Piperacillin/tazobactam, Amox/clav=Amoxicillin/clavulanate, TMP/SMX=Trimethoprim/sulfamethoxazole.

Table 2. Activity of selected antimicrobial agents when tested against 7,463 Gram-negative pathogens from European nations (2011).

Organism (no. tested) / Antimicrobial agent	MIC (mg/L) 50%	90%	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
E. coli (2,115)					
Amp/sulb	16	>32	0.5 – >32	41.2 / 38.8	41.2 / 58.8
Cefoperazone	2	>32	≤0.25 – >32	72.7 / 24.0	- / -
Cefo/sulb[b]	1	16	≤0.25 – >32	95.2 / 1.5	- / -
Pip/taz	2	32	≤0.5 – >64	89.6 / 5.3	85.0 / 10.4
Tigecycline[c]	0.12	0.25	≤0.03 – 1	100.0 / 0.0	100.0 / 0.0
Amikacin	2	8	0.5 – >32	98.6 / 0.5	95.7 / 1.4
Amox/clav	8	>8	≤1 – >8	67.8 / 32.2	67.8 / 32.2
Ampicillin	>8	>8	0.5 – >8	34.1 / 65.9	34.1 / 65.9
Cefepime	≤0.5	>16	≤0.5 – >16	86.4 / 12.0	82.0 / 15.1
Ceftazidime	0.12	16	0.03 – >32	86.2 / 11.7	81.7 / 13.8
Ceftriaxone	≤0.06	>8	≤0.06 – >8	80.8 / 18.9	80.8 / 18.9
Gentamicin	≤1	>8	≤1 – >8	86.0 / 13.8	85.1 / 14.0
Levofloxacin	≤0.12	>4	≤0.12 – >4	68.0 / 29.4	67.5 / 32.0
Meropenem	≤0.06	≤0.06	≤0.06 – >8	99.9 / 0.1	99.9 / <0.1
Tetracycline	2	>8	≤0.25 – >8	56.4 / 43.5	- / -
Tobramycin	1	>16	0.25 – >16	81.5 / 15.4	80.2 / 18.5
TMP/SMX	≤0.5	>4	≤0.5 – >4	60.0 / 40.0	60.0 / 39.9
Klebsiella spp. (1,076)[d]					
Amp/sulb	32	>32	1 – >32	41.2 / 50.8	41.2 / 58.8
Cefoperazone	8	>32	≤0.25 – >32	52.7 / 45.4	- / -
Cefo/sulb[b]	2	>32	≤0.25 – >32	76.2 / 15.1	- / -
Pip/taz	8	>64	≤0.5 – >64	66.9 / 22.7	59.6 / 33.1
Tigecycline[c]	0.25	1	0.06 – 4	99.0 / 0.0	95.8 / 1.0
Amikacin	2	16	≤0.25 – >32	90.9 / 3.3	83.6 / 9.1
Amox/clav	8	>8	≤1 – >8	54.2 / 45.8	54.2 / 45.8
Cefepime	≤0.5	>16	≤0.5 – >16	65.9 / 30.8	58.6 / 37.1
Ceftazidime	0.5	>32	0.03 – >32	60.2 / 36.2	56.7 / 39.8
Ceftriaxone	0.12	>8	≤0.06 – >8	56.7 / 42.9	56.7 / 42.9
Gentamicin	≤1	>8	≤1 – >8	73.1 / 25.6	71.7 / 26.9
Levofloxacin	0.25	>4	≤0.12 – >4	67.9 / 26.3	65.6 / 32.1
Meropenem	≤0.06	0.5	≤0.06 – >8	91.3 / 8.5	91.5 / 6.7
Tetracycline	2	>8	≤0.25 – >8	67.4 / 27.3	- / -
Tobramycin	0.5	>16	≤0.12 – >16	60.9 / 36.3	59.7 / 39.1
TMP/SMX	≤0.5	>4	≤0.5 – >4	62.0 / 38.0	62.0 / 37.3
Enterobacter spp.(578)[e]					
Cefoperazone	0.5	>32	≤0.25 – >32	72.8 / 24.6	- / -
Cefo/sulb[b]	0.5	32	≤0.25 – >32	88.9 / 5.4	- / -
Pip/taz	4	64	≤0.5 – >64	78.5 / 9.7	74.4 / 21.5
Tigecycline[c]	0.25	0.5	0.06 – >4	98.8 / 0.2	94.8 / 1.2
Amikacin	1	4	0.5 – >32	96.2 / 3.5	94.3 / 3.8
Cefepime	≤0.5	16	≤0.5 – >16	89.8 / 8.8	80.5 / 11.6
Ceftazidime	0.25	>32	0.06 – >32	70.1 / 27.0	66.8 / 29.9
Ceftriaxone	0.25	>8	≤0.06 – >8	65.2 / 32.2	65.2 / 32.2
Gentamicin	≤1	>8	≤1 – >8	88.6 / 10.6	87.5 / 11.4
Levofloxacin	≤0.12	4	≤0.12 – >4	89.1 / 9.0	86.7 / 10.9
Meropenem	≤0.06	0.12	≤0.06 – >8	96.9 / 1.7	98.3 / 0.9
Tetracycline	2	>8	0.5 – >8	85.3 / 12.3	- / -
Tobramycin	0.5	16	≤0.12 – >16	86.2 / 12.1	85.3 / 13.8
TMP/SMX	≤0.5	>4	≤0.5 – >4	83.7 / 16.3	83.7 / 16.1
Indole-positive *Proteus* spp. (234)[f]					
Cefoperazone	2	>32	≤0.25 – >32	82.9 / 14.1	- / -
Cefo/sulb[b]	1	4	≤0.25 – >32	99.6 / 0.4	- / -
Pip/taz	≤0.5	2	≤0.5 – >64	98.7 / 0.9	97.0 / 1.3
Tigecycline[c]	0.5	2	0.12 – >4	96.6 / 0.4	87.6 / 3.4
Amikacin	2	4	≤0.25 – >32	97.9 / 1.7	96.2 / 2.1
Cefepime	≤0.5	≤0.5	≤0.5 – >16	96.2 / 3.8	93.2 / 4.7
Ceftazidime	0.12	8	≤0.015 – >32	88.5 / 9.0	80.3 / 11.5
Ceftriaxone	≤0.06	4	≤0.06 – >8	79.5 / 15.4	79.5 / 15.4
Gentamicin	≤1	>8	≤1 – >8	84.5 / 11.2	80.3 / 15.5
Imipenem	2	2	≤0.12 – >8	32.1 / 9.8	90.2 / 0.4
Levofloxacin	≤0.12	>4	≤0.12 – >4	84.2 / 11.1	77.4 / 15.8
Meropenem	≤0.06	0.12	≤0.06 – 2	99.6 / 0.0	100.0 / 0.0
Tobramycin	1	8	≤0.12 – >16	88.0 / 6.8	83.3 / 12.0
TMP/SMX	≤0.5	>4	≤0.5 – >4	73.5 / 26.5	73.5 / 25.2
P. mirabilis (287)					
Amp/sulb	2	32	0.5 – >32	68.6 / 19.9	68.6 / 31.4
Cefoperazone	1	>32	≤0.25 – >32	77.7 / 18.1	- / -
Cefo/sulb[b]	1	8	≤0.25 – 32	99.7 / 0.0	- / -
Pip/taz	≤0.5	2	≤0.5 – >64	98.6 / 0.7	98.3 / 1.4
Tigecycline[c]	2	4	0.25 – >4	86.4 / 1.4	38.0 / 13.6
Amikacin	4	8	1 – >32	98.6 / 1.0	96.5 / 1.4
Amox/clav	2	>8	≤1 – >8	84.3 / 15.7	84.3 / 15.7
Ampicillin	>8	>8	0.5 – >8	48.8 / 51.2	48.8 / 51.2
Cefepime	≤0.5	2	≤0.5 – >16	93.7 / 6.3	89.9 / 6.6
Ceftazidime	0.06	2	≤0.015 – >32	93.4 / 4.9	89.9 / 6.6
Ceftriaxone	≤0.06	8	≤0.06 – >8	85.4 / 13.6	85.4 / 13.6
Gentamicin	≤1	>8	≤1 – >8	79.8 / 18.8	78.0 / 20.2
Imipenem	1	2	≤0.12 – >8	66.9 / 4.2	95.8 / 0.3
Levofloxacin	≤0.12	>4	≤0.12 – >4	84.6 / 13.6	75.9 / 15.4
Meropenem	≤0.06	0.12	≤0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
Tobramycin	1	8	0.25 – >16	85.0 / 8.0	77.0 / 15.0
TMP/SMX	≤0.5	>4	≤0.5 – >4	58.2 / 41.8	58.2 / 38.3

Organism (no. tested) / Antimicrobial agent	MIC (mg/L) 50%	90%	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
Serratia spp. (296)[g]					
Cefoperazone	2	32	≤0.25 – >32	87.5 / 9.8	- / -
Cefo/sulb[b]	2	16	≤0.25 – >32	94.9 / 1.7	- / -
Pip/taz	2	16	≤0.5 – >64	92.6 / 2.0	88.9 / 7.4
Tigecycline[c]	0.5	1	0.06 – 4	99.3 / 0.0	95.9 / 0.7
Amikacin	2	4	0.5 – >32	98.0 / 1.4	96.6 / 2.0
Cefepime	≤0.5	1	≤0.5 – >16	96.3 / 3.4	91.9 / 4.7
Ceftazidime	0.12	1	0.03 – >32	94.9 / 4.4	92.9 / 5.1
Ceftriaxone	0.25	>8	≤0.06 – >8	81.8 / 15.2	81.8 / 15.2
Gentamicin	≤1	2	≤1 – >8	93.9 / 5.8	92.9 / 6.1
Levofloxacin	≤0.12	1	≤0.12 – >4	94.9 / 3.4	91.2 / 5.1
Meropenem	≤0.06	≤0.06	≤0.06 – >8	98.3 / 1.7	98.3 / 0.3
Tobramycin	2	4	0.25 – >16	91.9 / 6.8	70.6 / 8.1
TMP/SMX	≤0.5	1	≤0.5 – >4	93.9 / 6.1	93.9 / 4.7
Citrobacter spp. (208)[h]					
Cefoperazone	0.5	>32	≤0.25 – >32	75.0 / 22.6	- / -
Cefo/sulb[b]	0.5	16	≤0.25 – >32	93.8 / 1.9	- / -
Pip/taz	2	64	≤0.5 – >64	82.2 / 5.8	77.4 / 17.8
Tigecycline[c]	0.12	0.25	0.06 – 4	99.5 / 0.0	98.6 / 0.5
Ampicillin	>8	>8	2 – >8	12.0 / 88.0	12.0 / 88.0
Cefepime	≤0.5	2	≤0.5 – >16	94.7 / 5.3	88.5 / 5.8
Ceftazidime	0.25	>32	0.06 – >32	77.4 / 21.2	75.0 / 22.6
Ceftriaxone	0.12	>8	≤0.06 – >8	74.5 / 24.5	74.5 / 24.5
Gentamicin	≤1	2	≤1 – >8	91.8 / 7.7	90.9 / 8.2
Levofloxacin	≤0.12	1	≤0.12 – >4	92.3 / 6.7	90.4 / 7.7
Meropenem	≤0.06	≤0.06	≤0.06 – >8	99.0 / 1.0	99.0 / 0.5
Tetracycline	1	4	0.5 – >8	90.4 / 9.1	- / -
Tobramycin	0.5	16	≤0.12 – >16	88.5 / 10.1	87.5 / 11.5
TMP/SMX	≤0.5	>4	≤0.5 – >4	86.1 / 13.9	86.1 / 13.9
H. influenzae (786)					
Pip/taz	≤0.5	≤0.5	≤0.5 – 1	100.0 / 0.0	- / -
Tigecycline[c]	0.25	0.5	≤0.015 – 2	86.8 / -	- / -
Amox/clav	≤1	≤1	≤1 – 8	99.9 / 0.1	99.4 / 0.6
Ampicillin	0.25	>8	≤0.12 – >8	85.1 / 12.9	85.1 / 14.9
Cefepime	≤0.5	≤0.5	≤0.5 – 1	100.0 / -	99.7 / 0.3
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.12	100.0 / -	100.0 / 0.0
Levofloxacin	≤0.12	≤0.12	≤0.12 – >4	99.9 / -	99.9 / 0.1
Meropenem	≤0.06	0.12	≤0.06 – 1	99.9 / -	100.0 / 0.0
Tetracycline	0.5	0.5	≤0.12 – >16	98.1 / 1.8	97.6 / 1.9
TMP/SMX	≤0.5	>4	≤0.5 – >4	71.1 / 24.3	71.1 / 27.4
H. parainfluenzae (44)					
Pip/taz	≤0.5	≤0.5	≤0.5 – 4	97.7 / 2.3	- / -
Tigecycline[c]	0.25	0.5	0.06 – 1	54.5 / -	- / -
Amox/clav	≤1	≤1	≤1 – 2	100.0 / 0.0	- / -
Ampicillin	0.25	2	≤0.12 – >8	88.6 / 9.1	- / -
Cefepime	≤0.5	≤0.5	≤0.5 – 4	95.5 / -	- / -
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.5	100.0 / -	- / -
Ciprofloxacin	≤0.03	≤0.03	≤0.03 – >4	97.7 / -	- / -
Gentamicin	≤1	2	≤1 – 4	- / -	- / -
Levofloxacin	≤0.12	≤0.12	≤0.12 – >4	97.7 / -	- / -
Meropenem	≤0.06	≤0.06	≤0.06 – 0.25	100.0 / -	- / -
Tetracycline	0.5	16	0.25 – >16	84.1 / 15.9	- / -
TMP/SMX	≤0.5	>4	≤0.5 – >4	75.0 / 18.2	- / -
M. catarrhalis (182)					
Pip/taz	≤0.5	≤0.5	≤0.5	- / -	- / -
Tigecycline[c]	0.06	0.06	≤0.015 – 0.25	- / -	- / -
Amox/clav	≤1	≤1	≤1	100.0 / 0.0	100.0 / 0.0
Cefepime	≤0.5	2	≤0.5 – 4	- / -	100.0 / 0.0
Ceftriaxone	0.25	0.5	≤0.06 – 2	100.0 / -	98.9 / 0.0
Ciprofloxacin	≤0.03	≤0.03	≤0.03 – 0.12	100.0 / -	100.0 / 0.0
Levofloxacin	≤0.12	≤0.12	≤0.12	100.0 / -	100.0 / 0.0
Meropenem	≤0.06	≤0.06	≤0.06 – 0.12	- / -	100.0 / 0.0
Tetracycline	0.25	0.25	≤0.12 – 2	100.0 / 0.0	99.5 / 0.0
TMP/SMX	≤0.5	≤0.5	≤0.5 – 4	96.7 / 0.5	96.7 / 1.6
Pseudomonas aeruginosa (1,185)					
Cefoperazone[b]	16	>32	0.5 – >32	54.3 / 35.6	- / -
Cefo/sulb	16	>32	0.5 – >32	63.5 / 21.2	- / -
Pip/taz	8	>64	≤0.5 – >64	61.2 / 18.7	61.2 / 38.8
Amikacin	4	>32	≤0.25 – >32	80.6 / 14.7	77.5 / 19.4
Cefepime	4	>16	≤0.5 – >16	69.5 / 17.8	69.5 / 30.5
Ceftazidime	4	>32	0.25 – >32	65.1 / 27.4	65.1 / 34.9
Colistin	1	2	≤0.25 – >4	99.6 / 0.3	99.6 / 0.4
Gentamicin	2	>8	≤1 – >8	70.3 / 27.2	70.3 / 29.7
Imipenem	1	>8	≤0.12 – >8	61.4 / 33.6	66.4 / 21.0
Levofloxacin	1	>4	≤0.12 – >4	60.3 / 33.9	52.0 / 39.7
Meropenem	1	>8	≤0.06 – >8	63.8 / 26.6	63.8 / 17.4
Tobramycin	0.5	>16	≤0.12 – >16	71.9 / 26.8	71.9 / 28.1
Acinetobacter spp.[i] (472)					
Amp/sulb	32	>32	≤0.25 – >32	31.4 / 61.9	- / -
Cefo/sulb	16	>32	≤0.25 – >32	52.5 / 20.3	- / -
Tigecycline	1	2	≤0.03 – >4	- / -	- / -
Amikacin	>32	>32	0.5 – >32	39.2 / 56.6	37.5 / 60.8
Colistin	1	2	≤0.25 – >4	99.2 / 0.8	99.2 / 0.8
Doxycycline	4	>8	≤0.06 – >8	51.6 / 48.2	- / -
Gentamicin	>8	>8	≤1 – >8	31.8 / 64.2	31.8 / 68.2
Imipenem	>8	>8	≤0.12 – >8	39.8 / 58.7	38.8 / 58.7
Meropenem	>8	>8	≤0.06 – >8	37.3 / 56.6	32.6 / 56.6
Tobramycin	2	>16	≤0.12 – >16	59.1 / 38.8	59.1 / 40.9
TMP/SMX	>4	>4	≤0.5 – >4	38.8 / 61.2	38.8 / 58.1

a. Criteria as published by the CLSI [2013] and EUCAST [2013].
b. Criteria as published by the CLSI [2013] for Cefoperazone used for Cefoperazone/sulbactam.
c. US-FDA breakpoints were applied when available [Tygacil Product Insert, 2012].
d. Includes: *Klebsiella oxytoca* (165 strains), *K. ozaenae* (one strain), *K. pneumoniae* (862 strains), and unspeciated *Klebsiella* (48 strains).
e. Includes: *Enterobacter aerogenes* (98 strains), *E. amnigenus* (three strains), *E. asburiae* (three strains), *E. cloacae* (429 strains), *E. intermedius* (one strain), *E. kobei* (three strains), *E. sakazakii* (one strain), and unspeciated *Enterobacter* (40 strains).
f. Includes: *Morganella morganii* (171 strains), *Proteus vulgaris* (24 strains), *Providencia rettgeri* (13 strains), *P. stuartii* (14 strains), unspeciated *Morganella* (one strain), unspeciated *Proteus* (10 strains), and unspeciated *Providencia* (one strain).
g. Includes: *Serratia ficaria* (one strain), *S. liquefaciens* (nine strains), *S. marcescens* (278 strains), *S. rubidaea* (one strain), and unspeciated *Serratia* (seven strains).
h. Includes: *Citrobacter braakii* (12 strains), *C. fameri* (two strains), *C. freundii* (100 strains), *C. koseri* (79 strains), *C. sedlakii* (one strain), *C. youngae* (two strains), and unspeciated *Citrobacter* (12 strains).
i. Includes: *Acinetobacter baumannii* (403 strains), *A. haemolyticus* (one strain), *A. junii* (two strains), *A. lwoffii* (13 strains), *A.ursingii* (two strains), and unspeciated *Acinetobacter* (51 strains). Only agents with >30% susceptibility rates are shown.
Abbreviations: Amb/sulb=Ampillicin/sulbactam, Cefo/sulb=Cefoperazone/sulbactam, Pip/taz=Piperacillin/tazobactam, Amox/clav=Amoxicillin/clavulanate, TMP/SMX=Trimethoprim/sulfamethoxazole.

Table 3. Activity of 12 selected antimicrobial agents when tested against ESBL-phenotype *Escherichia coli* and *Klebsiella* spp. isolated in European medical centres (918 strains cultured in 2011).

Organism (no. tested) / Antimicrobial agent	MIC (mg/L) 50%	90%	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
E. coli (426)					
Cefo/sulb[b]	8	32	≤0.25 – >32	81.0 / 6.3	- / -
Pip/taz	8	>64	≤0.5 – >64	74.4 / 11.7	60.1 / 25.6
Tigecycline[c]	0.12	0.25	≤0.03 – 0.5	100.0 / 0.0	100.0 / 0.0
Amikacin	4	16	0.5 – >32	94.1 / 2.6	83.3 / 5.9
Cefepime	>16	>16	≤0.5 – >16	32.9 / 59.4	15.5 / 73.7
Colistin	0.5	0.5	≤0.25 – 2	- / -	100.0 / 0.0
Gentamicin	2	>8	≤1 – >8	58.8 / 40.2	57.4 / 41.2
Levofloxacin	>4	>4	≤0.12 – >4	25.6 / 71.6	24.9 / 74.4
Meropenem	≤0.06	≤0.06	≤0.06 – >8	99.3 / 0.5	99.5 / 0.2
Tetracycline	>8	>8	1 – >8	32.6 / 66.9	- / -
Tobramycin	16	>16	0.25 – >16	42.3 / 52.6	41.5 / 57.7
TMP/SMX	>4	>4	≤0.5 – >4	35.4 / 64.6	35.4 / 64.3
Klebsiella spp. (492)[d]					
Cefo/sulb[b]	32	>32	0.5 – >32	49.4 / 32.7	- / -
Pip/taz	64	>64	2 – >64	34.4 / 46.5	22.2 / 65.7
Tigecycline[c]	0.25	1	0.06 – 4	98.4 / 0.0	93.7 / 1.6
Amikacin	4	32	0.5 – >32	80.1 / 7.3	64.6 / 19.9
Cefepime	>16	>16	≤0.5 – >16	25.4 / 67.3	10.6 / 81.1
Colistin	0.5	1	≤0.25 – >4	- / -	94.3 / 5.7
Gentamicin	>8	>8	≤1 – >8	44.9 / 52.8	41.9 / 55.1
Levofloxacin	>4	>4	≤0.12 – >4	35.6 / 54.3	31.3 / 64.4
Meropenem	≤0.06	>8	≤0.06 – >8	80.9 / 18.5	81.5 / 14.6
Tetracycline	8	>8	0.5 – >8	45.7 / 44.9	- / -
Tobramycin	>16	>16	0.25 – >16	18.7 / 75.8	17.3 / 81.3
TMP/SMX	>4	>4	≤0.5 – >4	28.0 / 72.0	28.0 / 70.9

a. Criteria as published by the CLSI [2013] and EUCAST [2013].
b. Criteria as published by the CLSI [2013] for Cefoperazone used for Cefoperazone/sulbactam.
c. USA-FDA breakpoints were applied when available [Tygacil Product Insert, 2012].
d. Includes: *Klebsiella oxytoca* (37 strains), *K. ozaenae* (one strain), *K. pneumoniae* (443 strains), and unspeciated *Klebsiella* (11 strains).
Abbreviations: Cefo/sulb=Cefoperazone/sulbactam, Pip/taz=Piperacillin/tazobactam, TMP/SMX=Trimethoprim/sulfamethoxazole.