Emerging Markets Resistance Surveillance Programme Report for 12 Asia-Pacific Nations (2011)

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Abstract

Objective: The EMRS program monitored susceptibility (S) rates and developing resistance (R) in 12 selected nations by geographic region including Asia-Pacific (APAC) nations (Australia [AUS], Hong Kong, India, Indonesia, Japan, Korea [KOR], Malaysia, New Zealand, Philippines [PHI], Singapore, Taiwan [TW] and Thailand).

Methods: Reference broth microdilution S methods and interpretations (CLSI, EUCAST) were applied, processing 5,053 strains (ranging from 137 [TW] to 1,136 [AUS] per country; 26 sites) with analysis of: *S. aureus* (SA; 1046), *S. pneumoniae* (SPN; 419), β-haemolytic (286) and viridans gr. strept (183), *E. coli* (EC; 501), *P. aeruginosa* (PSA; 430), *Klebsiella* spp. (KSP; 361) and Acinetobacter spp. (ACB; 243). Commonly marketed agents tested were: linezolid (LZD), vancomycin (VAN), tigecycline (TIG), colistin (COL), piperacillin/tazobactam (P/T), cefoperazone/sulbactam (C/S), amikacin (AMK), levofloxacin (LEV). Isolates were mainly from blood, respiratory tract and skin infections (17, 28 and 17%, respectively).

Results: Among SA (37% MRSA, highest in KOR [73%]), LZD, TIG and VAN were 100% active, but 7, 33 and 34% of strains were TMP/SMX-, LEV- or macrolide -R, respectively. Enterococci were dominantly LZD-, VAN-, and TIG-S (≥95%). SPN were most R to β-lactams and macrolides (45% R for both); and LZD-, LEV- and TIG-S (>98%). ESBL rates in EC and KSP were 48 and 47%, respectively; highest in TW at 75-91%. Best anti-ESBL agents were AMK (81-96% S), COL (>98%), TIG (>98%) and carbapenems (81-97%; NDM-1 and IMP-26 were detected in 3 EC and 1 KSP from PHI). PSA showed ≥20% R to all drugs except COL (99% S). Only two agents (COL [99%S] and TIG [93% at ≤2mg/L]) had more than 39% S rates for ACB.

Conclusions: Endemic and evolving R in EMRS monitored APAC nations showed compromised roles for many products. Among GP species, only LZD, TIG and glycopeptides remain potent. In contrast, for Enterobacteriaceae ESBLs and carbapenem-R limit choices to some older agents (AMK, COL, C/S, TIG); and fewer agents for PSA and ACB infections.

Introduction

The Emerging Market Resistance Surveillance (EMRS) programme was organized in the Asia-Pacific (APAC) region to supplement sampling for four nations: China (see companion ISAAR paper no. 113), Indonesia, Philippines and Thailand for 2011. These 16 additional sampling sites contributed 100-250 isolates across specified Gram-positive and -negative pathogen groups. Nine other nations were also sampled (Australia, Hong Kong, India, Japan, Korea, Malaysia, New Zealand, Singapore and Taiwan) with organisms referred to a central monitoring laboratory for reference (CLSI) testing against more than 30 antimicrobial agents and follow-up molecular procedures. The focus of the surveillance was to recognize and quantitate the level of resistances to commonly used, generally older, cost effective antimicrobials; and where possible characterize the resistance mechanisms and trends.

The APAC region historically has among the highest levels of resistance for many Gram-positive pathogens (MRSA, VRE, penicillin-resistant pneumococci, fluoroquinolone-resistant streptococci) and Gram-negative bacilli (β-lactamase-producing Enterobacteriaceae and multidrug-resistant [MDR] non-fermentative species). However, the resistance rates between nations within the region can be diverse, generally lower in Japan and Australia/New Zealand; and more elevated in East Asia and the Asian Subcontinent countries. The results for 12 nations providing more detailed analysis of the EMRS sites (**Tables 2** and **3**) are presented.

Methods

A total of 5,053 strains were processed from the APAC region for 2011, with a distribution of 137 isolates from Taiwan to 1,136 samples from Australia (26 sites overall). The distribution of samples was: *Staphylococcus aureus* (SA; 1,046), *Streptococcus pneumoniae* (SPN; 419); β-haemolytic streptococci (βHS; 286), viridans group streptococci (VGS, 183), *Escherichia coli* (EC; 501), *Pseudomonas aeruginosa* (PSA; 430), *Klebsiella* spp. (KSP; 361) and *Acinetobacter* spp. (ACB; 243). The subset of EMRS site strains are tabulated in **Tables 2** and **3**.

Commonly marketed agents tested were: linezolid (LZD), vancomycin (VAN), tigecycline (TIG), colistin (COL), piperacillin/tazobactam (P/T), cefoperazone/sulbactam (C/S), amikacin (AMK), levofloxacin (LEV). Isolates were mainly from blood, respiratory tract and skin infections (17, 28 and 17%, respectively). Susceptibility to over 30 antimicrobial agents was determined by reference broth microdilution methods as described by the Clinical and Laboratory Standards Institute (CLSI, 2013). Quality control strains (*S. aureus* ATCC 25923 and 29213, *E. faecalis* ATCC 29212, *S. pneumoniae* ATCC 49619, *E. coli* ATCC 25922 and 35218, and *P. aeruginosa* ATCC 27853) were tested concurrently and all QC values were observed within CLSI control ranges. Screening tests for ESBLs were determined using CLSI-recommended breakpoints of ≥2 mg/L for ceftriaxone or ceftazidime or aztreonam. Carbapenem-non-susceptible concentrations were ≥2 mg/L for doripenem or imipenem or meropenem when testing Enterobacteriaceae (CRE); and ≥4 mg/L for doripenem or imipenem or meropenem when *P. aeruginosa* strains were processed. Organisms meeting these criteria were further tested by the Check-MDR CT101 kit (Wageningen, The Netherlands) microarray method to determine β-lactamase genes and selected isolates had gene sequencing performed.

Table 1. Key antimicrobial resistance patterns for the 12 monitored nations in the APAC region (26 sites; 5,053 strains).

Nation (no. sites)	ESBL (%)[a]		CARB-R (%)			VRE (%)		MRSA (%)		
	EC	KSP	KSP	PSA	COL/ TIG-S[b]	Total	VanA	Total	LZD-S	TIG-S
Australia (6)	12	15	0	16	100/98	25	0	26	100	100
Hong Kong (1)	46	23	0	17	100/100	0	-	28	100	100
India (5)	78	64	25	32	100/98	0	-	45	100	100
Indonesia* (1)	71	64	0	8	100/100	0	-	28	100	100
Japan[c] (2)	-	-	-	-	-/-	0	-	41	100	100
Korea (2)	37	40	0	43	100/94	26	80	73	100	100
Malaysia (1)	36	45	0	24	100/96	-	-	32	100	100
N. Zealand (2)	11	10	0	6	100/100	0	-	9	100	100
Philippines* (1)	47[d]	55[d]	5[d]	50	100/95	0	-	59	100	100
Singapore (1)	21	32	0	22	100/96	-	-	52	100	100
Taiwan (1)	91	75	10	0	90/100	-	-	-	-	-
Thailand* (3)	41	44	3	30	94/100	0	-	46	100	100
All (26)	48	47	9	26	99/98	5[e]	50	37	100	100

a. EC=*E. coli*; KSP=*Klebsiella* spp.; TIG=tigecycline; COL=colistin; CARB=carbapenem; VRE=vancomycin-R enterococci;
b. Among KSP.
c. Only Gram-positive cocci were sampled.
d. Includes two NDM-1 and two IMP-26 in EC and KSP.
e. All *E. faecium*.
*=EMRS study subset

Results

- **Table 1** provides a general overview of key antimicrobial resistances among the 12 monitored nations (three were EMRS countries). These data revealed:
  - ESBL rates for EC/KSP ranged from 11/10% (New Zealand) to 91/75% (Taiwan); APAC average at 48%.
  - Carbapenem resistance (CARB-R) rates for KSP ranged from 0% (seven nations) to 25% (India); APAC average at 9%. COL and TIG activity was highest (90-100% susceptible).
  - PSA with CARB-R was 26% overall, highest in the Philippines (50%).
  - VRE isolates were generally rare (5% overall) outside of Australia and Korea.
  - MRSA rates (37% overall) ranged widely from 9% (New Zealand) to 73% (Korea).
- **Table 2** shows the EMRS site results for Gram-positive cocci in the supplemental nations.
  - MRSA rate was nearly 52%, but daptomycin, LZD, glycopeptides and TIG inhibited all strains at CLSI or USA-FDA susceptible breakpoints.
  - 9.4% of CoNS were teicoplanin-resistant (EUCAST criteria).
  - No VRE were observed.
  - Macrolide-, clindamycin-, tetracycline- and LEV-resistant BHS were detected widely.
  - Ceftriaxone resistance in SPN was high (14.3%)!
  - Glycopeptides, LZD and TIG remained most active against all Gram-positive pathogens.
- **Table 3** illustrates the antimicrobial susceptibility of various Gram-negative pathogens isolated from the supplemental (EMRS) APAC sites.
  - EC ESBL rate was 60% (regional rate, 48%), highest in Indonesia at 71%. ESBL-KSP was at 47% (regional rate also at 47%), again highest rates observed in Indonesia (64%). AMK, COL, carbapenems and TIG exhibited best activity versus ESBL-producing Enterobacteriaceae.
  - CARB-R strains were noted among EC and KSP at rates of 1-5%. Of greatest interest were four strains from the Philippines, one *K. pneumoniae* with an IMP-26 and three EC containing IMP-26 (1) or NDM-1 (2) enzymes. Clonal dissemination was observed.
  - Few drugs were active against PSA (some aminoglycosides, COL, C/S, P/T, carbapenems and cefepime). Only COL (97% susceptible) and TIG (MIC_{90}, 2 mg/L) were significantly active against ACB.

Conclusions

- Resistance surveillance for the APAC region and the EMRS sites exhibit a wide variety of patterns among Gram-positive and -negative pathogens.
  - Numerous tested agents (glycopeptides, LZD, TIG) remain widely active against Gram-positive pathogens and resistant phenotypes.
  - β-lactamase-mediated resistances (ESBLs, carbapenamases including metallo-β-lactamases [IMP, NDM]) have compromised therapy of infections caused by Enterobacteriaceae and PSA.
  - ACB infection treatment is extremely limited to only polymyxins and possibly TIG.
- Emerging novel resistances and clonal spread of existing mechanisms requires continued. surveillance monitoring of the APAC region including uncommonly sampled nations that appear in this EMRS program. Clearly newer, novel antimicrobials associated with antimicrobial stewardship will be required to address these treatment concerns.

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Table 2. Comparative antimicrobial activity of selected agents tested against key Gram-positive pathogens for the APAC region EMRS Program (2011).

Organism (no. tested)/ antimicrobial agent	MIC (mg/L) 50%	90%	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
S. aureus (166)					
Ceftriaxone	>8	>8	2 – >8	48.2 / 51.8	48.2 / 51.8
Clindamycin	≤0.25	>2	≤0.25 – >2	66.3 / 33.7	65.7 / 33.7
Daptomycin	0.25	0.5	0.12 – 0.5	100.0 / -	100.0 / 0.0
Doxycycline	0.12	8	≤0.06 – >8	71.7 / 8.4	63.3 / 30.7
Erythromycin	0.25	>16	≤0.12 – >16	57.2 / 38.6	58.4 / 41.6
Levofloxacin	0.25	>4	≤0.12 – >4	62.0 / 36.1	62.0 / 36.1
Linezolid	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Meropenem	0.5	>8	≤0.06 – >8	48.2 / 51.8	48.2 / 51.8
Oxacillin	>2	>2	≤0.25 – >2	48.2 / 51.8	48.2 / 51.8
Teicoplanin	≤2	≤2	≤2 – 8	100.0 / 0.0	99.4 / 0.6
Tigecycline[b]	0.06	0.25	≤0.03 – 0.5	100.0 / -	100.0 / 0.0
TMP/SMX[c]	≤0.5	>4	≤0.5 – >4	88.6 / 11.4	88.6 / 10.8
Vancomycin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
CoNS (85)[d]					
Ceftriaxone	>8	>8	1 – >8	18.8 / 81.2	18.8 / 81.2
Clindamycin	≤0.25	>2	≤0.25 – >2	63.5 / 31.8	63.5 / 36.5
Daptomycin	0.5	0.5	0.12 – 1	100.0 / -	100.0 / 0.0
Doxycycline	0.5	2	≤0.06 – >8	94.1 / 1.2	74.1 / 8.2
Erythromycin	>16	>16	≤0.12 – >16	35.3 / 64.7	35.3 / 64.7
Levofloxacin	4	>4	≤0.12 – >4	42.4 / 56.5	42.4 / 56.5
Linezolid	0.5	1	0.25 – 1	100.0 / 0.0	100.0 / 0.0
Meropenem	2	>8	≤0.06 – >8	18.8 / 81.2	18.8 / 81.2
Oxacillin	>2	>2	≤0.25 – >2	18.8 / 81.2	18.8 / 81.2
Teicoplanin	≤2	4	≤2 – 16	95.3 / 0.0	90.6 / 9.4
Tigecycline[b]	0.06	0.12	≤0.03 – 0.25	- / -	100.0 / 0.0
TMP/SMX[c]	≤0.5	>4	≤0.5 – >4	64.7 / 35.3	64.7 / 28.2
Vancomycin	1	2	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Enterococci (54)[e]					
Ampicillin	1	>8	0.5 – >8	68.5 / 31.5	68.5 / 31.5
Daptomycin	1	2	0.25 – 4	100.0 / -	- / -
Doxycycline	8	>8	≤0.06 – >8	31.5 / 31.5	- / -
Imipenem	1	>8	0.25 – >8	- / -	66.7 / 33.3
Levofloxacin	>4	>4	0.5 – >4	44.4 / 53.7	- / -
Linezolid	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Teicoplanin	≤2	≤2	≤2	100.0 / 0.0	100.0 / 0.0
Tigecycline[b]	0.06	0.06	≤0.03 – 0.12	100.0 / -	100.0 / 0.0
Vancomycin	1	2	0.5 – 2	100.0 / 0.0	100.0 / 0.0
S. pneumoniae (42)[f]					
Amox/clavulanate[g]	≤1	8	≤1 – >8	76.2 / 21.4	- / -
Ceftriaxone	≤0.06	8	≤0.06 – 8	78.6 / 14.3	66.7 / 14.3
Clindamycin	≤0.25	>2	≤0.25 – >2	50.0 / 50.0	50.0 / 50.0
Erythromycin	1	>16	≤0.12 – >16	47.6 / 52.4	47.6 / 52.4
Levofloxacin	1	1	0.5 – 2	100.0 / 0.0	100.0 / 0.0
Linezolid	0.5	1	0.25 – 1	100.0 / -	100.0 / 0.0
Penicillin[h]	≤0.06	4	≤0.06 – 8	76.2 / 4.8	- / -
Tetracycline	>8	>8	≤0.25 – >8	28.6 / 69.0	28.6 / 71.4
Tigecycline[b]	≤0.03	≤0.03	≤0.03 – 0.06	100.0 / -	- / -
TMP/SMX[c]	≤0.5	>4	≤0.5 – >4	50.0 / 40.5	57.1 / 40.5
Vancomycin	0.25	0.5	0.25 – 0.5	100.0 / -	100.0 / 0.0
β-haemolytic streptococci (27)[i]					
Ceftriaxone	≤0.06	0.12	≤0.06 – 0.25	100.0 / -	100.0 / 0.0
Clindamycin	≤0.25	>2	≤0.25 – >2	66.7 / 33.3	66.7 / 33.3
Daptomycin	0.12	0.25	≤0.06 – 0.5	100.0 / -	100.0 / 0.0
Erythromycin	≤0.12	>16	≤0.12 – >16	55.6 / 37.0	55.6 / 37.0
Levofloxacin	0.5	1	0.25 – >4	96.3 / 3.7	92.6 / 3.7
Linezolid	1	1	0.5 – 1	100.0 / -	100.0 / 0.0
Penicillin	≤0.06	≤0.06	≤0.06	100.0 / -	100.0 / 0.0
Tetracycline	>8	>8	≤0.25 – >8	14.8 / 81.5	14.8 / 85.2
Tigecycline[b]	≤0.03	0.12	≤0.03 – 0.12	100.0 / -	100.0 / 0.0
TMP/SMX[c]	≤0.5	≤0.5	≤0.5	- / -	100.0 / 0.0
Vancomycin	0.5	0.5	0.25 – 1	100.0 / -	100.0 / 0.0
Viridans group streptococci (10)[j]					
Ceftriaxone	0.25	1	0.12 – 4	90.0 / 10.0	80.0 / 20.0
Clindamycin	≤0.25	>2	≤0.25 – >2	80.0 / 20.0	80.0 / 20.0
Daptomycin	0.5	1	0.12 – 1	100.0 / -	- / -
Erythromycin	≤0.12	>16	≤0.12 – >16	50.0 / 50.0	- / -
Levofloxacin	1	1	0.25 – 2	100.0 / 0.0	- / -
Linezolid	0.5	1	0.5 – 1	100.0 / -	- / -
Penicillin	0.12	0.5	≤0.06 – 4	50.0 / 10.0	60.0 / 10.0
Tetracycline	8	>8	0.5 – >8	40.0 / 60.0	- / -
Tigecycline[b]	≤0.03	≤0.03	≤0.03 – 0.25	100.0 / -	- / -
Vancomycin	0.5	0.5	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. Trimethoprim/sulfamethoxazole.
d. Includes: *Staphylococcus epidermidis* (three strains), *S. haemolyticus* (one strain), *S. hominis* (one strain), *S. warneri* (two strains), and unspecieated coagulase-negative staphylococci (78 strains).
e. Includes: *Enterococcus avium* (one strain), *E. faecalis* (35 strains), and *E. faecium* (18 strains).
f. 33.3% penicillin-non-susceptible.
g. Amoxicillin/clavulanate.
h. Criteria as published by the CLSI [2012] for 'Penicillin parenteral (non-meningitis)'.
i. Includes: *Streptococcus dysgalactiae* (six strains), Group A *Streptococcus* (five strains), Group B *Streptococcus* (11 strains), Group F *Streptococcus* (one strain), Group G *Streptococcus* (three strains), and unspecieated β-haemolytic streptococci (one strain).
j. Includes: *Streptococcus mitis* (one strain), *S. oralis* (one strain), *S. salivarius* (one strain), *S. sanguinis* (one strain), and unspecieated viridans group streptococci (6 strains).

Table 3. Comparisons of antimicrobial activity when testing Gram-negative pathogens in the EMRS program sites for the APAC region (2011).

Organism (no. tested) /antimicrobial agent	MIC (mg/L) 50%	90%	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
E. coli (all; 101)					
Amikacin	4	16	1 – >32	95.0 / 5.0	89.0 / 5.0
Ampicillin/sulbactam	16	>32	1 – >32	30.7 / 44.6	30.7 / 69.3
Cefepime	8	>16	≤0.5 – >16	55.4 / 36.6	48.5 / 50.5
Cefoperazone	>32	>32	≤0.25 – >32	44.0 / 54.0	- / -
Cef/sulbactam[b]	4	16	≤0.25 – >32	91.1 / 2.0	- / -
Ceftazidime	4	32	0.06 – >32	52.5 / 44.6	41.6 / 47.5
Ceftriaxone	>8	>8	≤0.06 – >8	40.6 / 59.4	40.6 / 59.4
Colistin	0.5	0.5	≤0.25 – >4	- / -	98.0 / 2.0
Gentamicin	2	>8	≤1 – >8	56.4 / 42.6	56.4 / 43.6
Imipenem	≤0.12	0.25	≤0.12 – 8	97.0 / 1.0	99.0 / 0.0
Levofloxacin	>4	>4	≤0.12 – >4	37.6 / 59.4	37.6 / 62.4
Meropenem	≤0.06	≤0.06	≤0.06 – >8	97.0 / 3.0	97.0 / 2.0
Piperacillin/tazobactam	2	16	≤0.5 – >64	91.1 / 3.0	82.2 / 8.9
Tetracycline	>8	>8	0.5 – >8	29.7 / 70.3	- / -
Tigecycline[c]	0.12	0.25	≤0.03 – 2	100.0 / 0.0	99.0 / 0.0
Tobramycin	4	>16	0.5 – >16	51.5 / 44.6	49.5 / 48.5
TMP/SMX[d]	>4	>4	≤0.5 – >4	35.6 / 64.4	35.6 / 63.4
ESBL-phenotype (61)[e]					
Amikacin	4	16	2 – >32	91.8 / 8.2	83.6 / 8.2
Cef/sulbactam[b]	8	32	≤0.25 – >32	85.2 / 3.3	- / -
Colistin	0.5	0.5	≤0.25 – >4	- / -	96.7 / 3.3
Imipenem	≤0.12	0.25	≤0.12 – 8	95.1 / 1.6	98.4 / 0.0
Meropenem	≤0.06	≤0.06	≤0.06 – >8	95.1 / 4.9	95.1 / 3.3
Piperacillin/tazobactam	4	32	1 – >64	85.2 / 4.9	73.8 / 14.8
Tigecycline[c]	0.12	0.12	≤0.03 – 2	100.0 / 0.0	98.4 / 0.0
Klebsiella spp. (all; 75)[f]					
Amikacin	2	8	0.5 – >32	97.3 / 2.7	96.0 / 2.7
Ampicillin/sulbactam	8	>32	0.5 – >32	50.7 / 40.0	50.7 / 49.3
Cefepime	≤0.5	>16	≤0.5 – >16	65.3 / 30.7	57.3 / 37.3
Cefoperazone	1	>32	≤0.25 – >32	57.3 / 41.3	- / -
Cef/sulbactam[b]	1	32	≤0.25 – >32	88.0 / 4.0	- / -
Ceftazidime	0.25	>32	0.06 – >32	65.3 / 30.7	58.7 / 34.7
Ceftriaxone	0.12	>8	≤0.06 – >8	53.3 / 46.7	53.3 / 46.7
Colistin	0.5	0.5	≤0.25 – 4	- / -	98.7 / 1.3
Gentamicin	≤1	>8	≤1 – >8	66.7 / 33.3	66.7 / 33.3
Imipenem	≤0.12	0.5	≤0.12 – 8	96.0 / 4.0	96.0 / 0.0
Levofloxacin	≤0.12	>4	≤0.12 – >4	84.0 / 12.0	81.3 / 16.0
Meropenem	≤0.06	≤0.06	≤0.06 – >8	94.7 / 5.3	94.7 / 4.0
Piperacillin/tazobactam	4	64	≤0.5 – >64	81.3 / 8.0	72.0 / 18.7
Tetracycline	2	>8	0.5 – >8	60.0 / 40.0	- / -
Tigecycline[c]	0.25	1	0.12 – 4	98.7 / 0.0	92.0 / 1.3
Tobramycin	0.5	>16	0.25 – >16	65.3 / 32.0	58.7 / 34.7
TMP/SMX[d]	≤0.5	>4	≤0.5 – >4	54.7 / 45.3	54.7 / 42.7
ESBL-phenotype (35)[e]					
Amikacin	4	8	1 – >32	94.3 / 5.7	91.4 / 5.7
Cef/sulbactam[b]	8	32	≤0.25 – >32	74.3 / 8.6	- / -
Colistin	0.5	2	≤0.25 – 4	- / -	97.1 / 2.9
Imipenem	≤0.12	1	≤0.12 – 8	91.4 / 8.6	91.4 / 0.0
Levofloxacin	0.5	>4	≤0.12 – >4	65.7 / 25.7	60.0 / 34.3
Meropenem	≤0.06	4	≤0.06 – >8	88.6 / 11.4	88.6 / 8.6
Piperacillin/tazobactam	16	>64	2 – >64	60.0 / 17.1	42.9 / 40.0
Tigecycline[c]	0.5	2	0.12 – 4	97.1 / 0.0	85.7 / 2.9
Enterobacter spp. (36)[g]					
Amikacin	2	8	1 – 16	100.0 / 0.0	97.2 / 0.0
Cefepime	4	>16	≤0.5 – >16	61.1 / 36.1	38.9 / 47.2
Cef/sulbactam[b]	8	>32	≤0.25 – >32	83.3 / 11.1	- / -
Colistin	0.5	>4	≤0.25 – >4	- / -	75.0 / 25.0
Gentamicin	4	>8	≤1 – >8	50.0 / 47.2	44.4 / 50.0
Imipenem	0.25	1	≤0.12 – 2	94.4 / 0.0	100.0 / 0.0
Levofloxacin	0.5	>4	≤0.12 – >4	77.8 / 19.4	69.4 / 22.2
Meropenem	≤0.06	0.12	≤0.06 – 0.5	100.0 / 0.0	100.0 / 0.0
Piperacillin/tazobactam	16	>64	1 – >64	55.6 / 19.4	47.2 / 44.4
Tetracycline	2	>8	0.5 – >8	52.8 / 44.4	- / -
Tigecycline[c]	0.25	2	0.12 – 4	91.7 / 0.0	88.9 / 8.3
TMP/SMX[d]	≤0.5	>4	≤0.5 – >4	52.8 / 47.2	52.8 / 47.2
P. aeruginosa (60)					
Amikacin	4	16	0.5 – >32	91.7 / 6.7	88.3 / 8.3
Cefepime	4	>16	1 – >16	71.7 / 18.3	71.7 / 28.3
Cef/sulbactam[b]	8	>32	1 – >32	66.7 / 11.7	- / -
Cefoperazone	8	>32	2 – >32	61.7 / 35.0	- / -
Ceftazidime	4	>32	1 – >32	70.0 / 28.3	70.0 / 30.0
Colistin	2	2	1 – 4	98.3 / 0.0	98.3 / 1.7
Gentamicin	2	>8	≤1 – >8	85.0 / 13.3	85.0 / 15.0
Imipenem	1	>8	0.5 – >8	71.7 / 28.3	71.7 / 13.3
Levofloxacin	0.5	>4	≤0.12 – >4	75.0 / 20.0	61.7 / 25.0
Meropenem	0.25	8	≤0.06 – >8	71.7 / 21.7	71.7 / 10.0
Piperacillin/tazobactam	8	>64	1 – >64	66.7 / 16.7	66.7 / 33.3
Tobramycin	0.5	16	0.25 – >16	85.0 / 13.3	85.0 / 15.0
Acinetobacter spp. (38)[h]					
Amikacin	16	>32	0.5 – >32	50.0 / 50.0	47.4 / 50.0
Cef/sulbactam[b]	16	>32	0.5 – >32	55.3 / 26.3	- / -
Colistin	1	2	0.5 – >4	97.4 / 2.6	97.4 / 2.6
Tigecycline	1	2	≤0.03 – 4	- / -	- / -

a. Criteria as published by the CLSI [2013] and EUCAST [2013].
b. Cefoperazone/sulbactam; 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. Trimethoprim/sulfamethoxazole.
e. Only drugs with ≥40% susceptibility are listed.
f. Includes: *Klebsiella oxytoca* (three strains), *K. pneumoniae* (53 strains), and unspecieated *Klebsiella* (19 strains).
g. Includes: *Enterobacter aerogenes* (five strains), *E. cloacae* (24 strains), *E. sakazakii* (one strain), and unspecieated *Enterobacter* spp. (six strains).
h. Only drugs active against ≥50% of strains are shown.