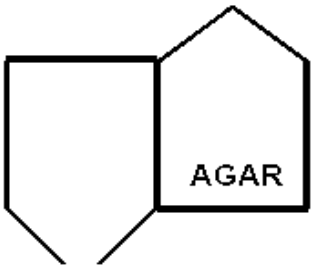

The Australian Group on Antimicrobial Resistance

Gram-negative Survey

2011 Antimicrobial Susceptibility Report

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On behalf of the Australian Group for Antimicrobial Resistance (AGAR)

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2 EXECUTIVE SUMMARY

The Australian Group on Antimicrobial Resistance (AGAR) performs regular period-prevalence studies to monitor changes in antimicrobial resistance. In 2008, AGAR moved to performing annual surveys of resistance in sentinel Gram-negative pathogens, alternating between pathogens causing community-onset infections and those causing hospital-onset infections, having previously conducted biennial surveys of all isolates regardless of infection onset. The 2011 survey focussed on hospital-onset infections, examining isolates from all specimens presumed to be causing disease. In all, 29 laboratories covering each state and mainland territory of Australia participated in the 2011 surveillance program. One thousand eight hundred and twenty-seven *E. coli*, 537 *Klebsiella* species and 269 *Enterobacter* species were tested using a commercial automated method (Vitek 2, BioMérieux). Results were analysed using CLSI breakpoints from January 2012.

The majority of isolates (>70%) were from urine specimens; 5.6% of isolates (n=148) came from blood cultures. Since the first hospital-onset survey in 2009, the following important changes have been noted: There has been a rise in the overall proportion of strains resistant to β-lactam agents. Most noticably, this appears to be related to the increase in CTX-M-type ESBL-producing strains in all species tested. As ESBL production is linked to gentamicin and ciprofloxacin resistance, resistances to these to agents has also risen since 2009. Although still comparatively uncommon, resistance to carbapenems appears to be slowly rising. This is attributed to the low slow dissemination of the carbepenemase encoded by $bla_{\text{IMP-4}}$ which was found in three states. Multi-resistance rates in *E. coli* and *Klebsiella* species have increased about 2% since 2009, comprising 14.2% and 10.6% respectively.

There are worrying trends in the expansion of third-generation cephalosporin resistance in hospital-onset *E. coli* and *Klebsiella* species especially those producing of CTX-M type enzymes, and early signs of the carbapenemase $bla_{\text{IMP-4}}$ spreading across the country. The increase in multi-resistance is another worrying trend, particularly the linked resistances of ESBL production, ciprofloxacin and gentamicin resistance.

3 BACKGROUND

3.1 OBJECTIVES OF THE PROGRAM

AGAR commenced surveillance of key Gram-negative pathogens, *Escherichia coli* and *Klebsiella* species in 1992. Surveys have been conducted biennially since then. In 2004, another genus of Gram-negative pathogens in which resistance can be of clinical importance, *Enterobacter* species, was added. In 2008, AGAR moved to performing annual surveys of resistance in sentinel Gram-negative pathogens, having previously conducted biennial surveys. Annual surveys alternate each year between pathogens causing community-onset infections and those causing hospital-onset infections. The objectives of the 2011 surveillance program were:

1. Determine proportions of resistance to the main therapeutic agents in *E. coli*, *Klebsiella* species, and *Enterobacter* species isolated from hospitalised inpatients
2. Examine the extent of co-resistance and multi-resistance in these species
3. Detect emerging resistance to extended-spectrum cephalosporins and newer last-line agents such as carbapenems

3.2 IMPORTANCE OF SPECIES SURVEYED

All species surveyed are members of the family Enterobacteriaceae. This family contains the most important Gram-negative pathogens in a wide range of common conditions in both the community and in hospitals. The three groups surveyed are considered to be valuable sentinels for multi-resistance and emerging resistance.

E. coli is the commonest cause of upper and lower urinary tract infection, and is prominent in a number of other conditions including intra-abdominal sepsis, post-operative wound infections and neonatal sepsis, cholangitis and septicaemia in the profoundly neutropenic patient. It is one of the commonest isolates in the routine microbiology laboratory.

Klebsiella species are associated with similar conditions to those of *E. coli* but occur less frequently. They are more likely than *E. coli* to acquire and transmit resistance determinants. They are in addition an important cause of pneumonia. This genus is usually intrinsically resistant to aminopenicillins through the possession of one of a small number of natural ß-lactamases, most commonly SHV-1.

Enterobacter species are predominantly hospital-acquired pathogens. They are intrinsically resistant to aminopenicillins, first and second generation cephalosporins including cefamycins. Hence, they are naturally multiresistant. They acquire resistance to important Gram-negative agents relatively easily, and can act as a reservoir for important resistance genes.

3.3 RELEVANCE OF ANTIMICROBIALS TESTED

3.3.1 B-LACTAMS

This group of agents are the **mainstay of treatment** for Gram-negative infections in all settings, being the drugs of choice for both minor outpatient infections (e.g. lower UTI), and serious community-acquired infections (e.g. septicaemia)

Ampicillin: an aminopenicillin, used to predict resistance to ampicillin and amoxycillin. Considered the drugs of choice for susceptible *E. coli.* [Parenteral, oral; widespread community, mainly as amoxycillin, and hospital use]

Amoxycillin-clavulanate: a ß-lactamase inhibitor combination. Multiple uses including infections caused by ampicillin-resistant strains of *E. coli* and *Klebsiella* species. [Oral, widespread hospital and community use]

Piperacillin-tazobactam: a ß-lactamase inhibitor combination. Broad spectrum agent with multiple uses including against Gram-negative bacteria resistant to other agents. Similar activity to ticarcillin-clavulanate, another widely used ß-lactamase inhibitor combination. [Parenteral, limited hospital use]

Cefazolin: first-generation cephalosporin used for treating common Gram-negative and Gram-positive pathogens. Cefazolin is an important agent for surgical prophylaxis and penicillin-allergic patients. [Parenteral, cephalexin is the nearest oral equivalent, widespread community and hospital use]

Cefoxitin: second-generation cephalosporin, although better described as a cephamycin due to its unique spectrum. Very limited clinical use in surgical prophylaxis. Used in this study to screen for potential AmpC ß-lactamases. [Parenteral, very limited hospital use]

Ceftriaxone: a third-generation cephalosporin. For Enterobacteriaceae, testing results predict cefotaxime. Multiple specialised clinical uses. [Parenteral, extensive hospital use, strictly avoided in some hospitals]

Ceftazidime: a third-generation cephalosporin but with additional antipseudomonal activity. Most susceptible to extended-spectrum ß-lactamases and included in this study for that reason. Main role in Australia as an antipseudomonal agent. [Parenteral, modest hospital use in specialized units]

Cefepime: a fourth generation cephalosporin, but with activity against organisms producing AmpC ß-lactamases, both natural (chromosomal cephalosporinases) and acquired. [Parenteral, modest hospital use in specialized units]

Meropenem: a carbapenem. Predicts activity of most of the other carbapenems, imipenem and doripenem, against Enterobacteriaceae. Last-line agent used for multi-resistant Gram-negative infections, presumptive and proven. [Parenteral, modest restricted hospital use]

Ertapenem: a carbapenem, was included for the first time in this survey. It has a narrower spectrum than meropenem (no activity against *Pseudomonas aeruginosa* or *Enterococcus* spp.) but is active against ESBL-producing Gram-negative bacteria and has the advantage of a long elimination half-life allowing once-daily dosing

3.3.2 OTHER ANTIMICROBIAL CLASSES

Ciprofloxacin: a fluoroquinolone. Predicts resistance in Gram-negatives to other fluoroquinolones, ofloxacin, moxifloxacin. Resistance to ciprofloxacin confirms resistance to norfloxacin. Valuable oral agent reserved for infections caused by Gram-negatives resistant to other antibacterials, and as an antipseudomonal. [Oral, IV, restricted community and hospital use]

Gentamicin: an aminoglycoside. Generally predicts resistance in Gram-negatives to tobramycin (but not Amikacin). Valuable first line agent for presumptive Gram-negative sepsis. [IV, high first line hospital use].

Amikacin: an aminoglycoside. It is unaffected by the common aminoglycoside-modifying enzymes that cause Gram-negative bacteria to become resistant to gentamicin and tobramycin.

Trimethoprim: a folate synthesis (dihydrofolate reductase) inhibitor. Standard treatment for uncomplicated urinary tract infection. [Oral, moderate community use, limited hospital use, both mainly as cotrimoxazole]

Nitrofurantoin: a nitrofuran. A unique mechanism of action but its role, based on its pharmacology, is restricted to the treatment and prevention of urinary tract infection.

3.4 RESISTANCES OF CONCERN

3.4.1 B-LACTAMASES

ß-lactamases are the principal resistance mechanism to ß-lactams in Gram-negative bacteria. There is an enormous range of these enzymes now described. Like antibiotics themselves, each ß-lactamase has a "spectrum" of ß-lactams that it can hydrolyze and inactivate. The ß-lactamases of worldwide importance are listed in Table 1.

Table 1 Important ß-lactamases in Enterobacteriaceae

ß-lactamase	Mainly found in	ß-lactams affected or usual co-resistances	Comments
TEM-1,2	*E. coli*	Ampicillin, amoxycillin, piperacillin, (cephalothin)	Very common
TEM-1 hyperproduction	*E. coli*	Amoxycillin-clavulanate (piperacillin-tazobactam)	Increased prevalence in recent years

ß-lactamase	Mainly found in	ß-lactams affected or usual co-resistances	Comments
TEM, SHV and CTX-M extended spectrum ß-lactamases (ESBLs)	*E. coli*, *K. pneumoniae, Enterobacter* spp.	Ampicillin, amoxycillin, piperacillin, first-, second- (excluding cephamycins (cefoxitin) and third generation cephalosporins, monobactam	Mainly hospital-associated until recent emergence in community practice overseas
K1 hyperproduction	*K. oxytoca*	Ampicillin, amoxicillin, piperacillin, first- and second-generation cephalosporins, aztreonam, ceftriaxone > cefotaxime	Natural enzyme selected to hyperproduction
Chromosomal cephalosporinases	ESCaPPM*	Ampicillin, amoxicillin, first-, second-generation cephalosporins, third generation cephalosporins in de-repressed mutants.	Natural enzymes. Selection for stably de-repressed mutants can occur during treatment and strains with this are common
Plasmid-borne AmpC ß-lactamases	*E. coli, K. pneumoniae*	Ampicillin, amoxycillin, first, second and third-generation cephalosporins, including cephamycin	Emerging overseas as a significant problem
Carbapenemases	Rare, but increasing	Ampicillin, amoxycillin, first-, second and third-generation cephalosporins +/-aztreonam	Have been rare in Enterobacteriaceae but now being seen for the first time in Australia and overseas

* ***E****nterobacter* species, ***S****erratia* species, ***C****itrob****a****cter freundii*, ***P****roteus vulgaris* and *penneri*, ***P****rovidencia* species and ***M****organella morganii*.

3.4.2 NON-BETA-LACTAM ANTIBIOTICS

In Enterobacteriaceae, resistance to fluoroquinolones such as ciprofloxacin is generally the result of mutations in the *gyrA* gene, leading to amino acid changes in the target protein DNA gyrase. Two or three mutation and amino acid changes are required to develop full resistance to ciprofloxacin. Occasionally resistance can be brought about through efflux, usually in combination with DNA gyrase mutations. Plasmid-mediated quinolone resistance is emerging, but is not addressed in this report.

Resistance to gentamicin and other aminoglycosides is most commonly the result of aminoglycoside modifying enzymes. The types prevalent in Enterobacteriaceae can vary widely by hospital, region and country.

Trimethoprim resistance is most commonly the result of mutations in the gene encoding the dihydrofolate reductase.

4 STUDY DESIGN

Twenty-nine institutions from each State and mainland Territories of Australia participated in the Gram-negative 2011 AGAR survey. Each institution collected up to 70 *E. coli*, 20 *Klebsiella* species, 10 *Enterobacter* species from different patients hospitalised for more than 48 hours.

Table 2. Isolates Tested

Region	Number of Institutions	*E. coli*	*Enterobacter* species	*Klebsiella* species	Total
New South Wales (NSW) Australian Capital Territory (ACT)	8	538	71	145	754
Northern Territory (NT) Queensland (QLD)	7	467	69	139	675
South Australia (SA)	3	163	30	50	243
Victoria (VIC) Tasmania (TAS)	7	381	60	123	564
Western Australia (WA)	4	278	39	80	397
Total	**29**	**1,827**	**269**	**537**	**2,633**

4.1 PARTICIPITATING INSTITUTIONS

ACT/NSW (8)

Concord Hospital
Douglass Hanly Moir
Nepean Hospital
Royal North Shore Hospital
Royal Prince Alfred Hospital
Sydney South West Pathology Services
The Canberra Hospital
Westmead Hospital

QLD/NT (7)

Pathology Queensland, Cairns Base Hospital
Pathology Queensland, Gold Coast Hospital
Pathology Queensland, Prince Charles Hospital
Pathology Queensland, Princess Alexandra Hospital
Pathology Queensland, Central Laboratory
Royal Darwin Hospital
Sullivan Nicolaides Pathology

SA (3)

SA Pathology - Flinders Medical Centre
SA Pathology - Royal Adelaide Hospital
SA Pathology - Women's and Children's Hospital

VIC/TAS (7)

Alfred Hospital
Austin Health
Launceston General Hospital
Monash Medical Centre
Royal Children's Hospital
Royal Hobart Hospital
St Vincent's Hospital

WA (4)
PathWest Laboratory Medicine - WA, Fremantle Hospital
PathWest Laboratory Medicine - WA, QEII Medical Centre
PathWest Laboratory Medicine - WA, Royal Perth Hospital
St John of God Pathology

4.2 METHODS

4.2.1 SPECIES IDENTIFICATION

E. coli isolates were identified by one of the following methods:

Vitek®, Phoenix™ Automated Microbiology System, MicroScan®, Microbact, or ATB®
Chromogenic agar plus spot indole (DMACA) (urinary tract isolates)
Agar replication
Minimum tests for urine isolates: BGA or citrate, indole and lactose fermentation.

Klebsiella species and *Enterobacter* species were identified by one of the following methods:

API20E, MicroScan®, Vitek® (plus indole), Phoenix™ Automated Microbiology System, or ATB®
Chromogenic agar plus spot indole (DMACA) (urinary tract isolates)
Agar replication

4.2.2 SPECIES INCLUDED IN STUDY

Table 3. Species included

Group	Organism		Total
E. coli	*E. coli*		1,827
Klebsiella	*K. pneumoniae*		396
	K. oxytoca		137
	K. pneumoniae subsp *ozaenae*		3
	Klebsiella not speciated.		1
		Total	537
Enterobacter	*E. cloacae*		180
	E. aerogenes		83
	E. asburiae		3
	E. gergoviae		2
	Enterobacter not speciated.		1
		Total	269

4.3 SUSCEPTIBILITY TESTING

4.3.1 METHOD

Testing was performed by a commercial semi-automated method, Vitek 2 (BioMérieux) which is calibrated to the ISO reference standard method of broth microdilution. Commercially available Vitek AST-N149 cards were utilized by all participants throughout the survey period. The CLSI breakpoints from Janurary 2012 have been employed in the analysis

4.3.2 ANTIBIOTICS TESTED

Table 4. Antimicrobials Tested

Antimicrobial Agent	AST N149 Concentration range	CLSI Breakpoints (mg/L)[a]		
Ampicillin	≤2, 4, 8, 16, ≥32	≤8	16	≥32
Co-amoxyclav	≤2/1, 4/2, 8/4, 16/8, ≥32/16	≤8/4	16/8	≥32/16
Piperacillin/tazobactam[b]	≤4/4, 8/4, 16/4, 32/4, 64/4, ≥128/4	≤16/4	32/4-64/4	≥128/4
Ticarcillin/clavulanate	≤8/2, 16/2, 32/2, 64/2, ≥128/2	≤16/2	32/2-64/2	≥128/2
Cefazolin[c]	≤4, 8, 16, 32, ≥64	≤2	4	≥8
Cefepime	≤1, 2, 4, 8, 16, 32, ≥64	≤8	16	≥32
Ceftriaxone	≤1, 2, 4, 8, 16, 32, ≥64	≤1	2	≥4
Cefoxitin	≤4, 8, 16, 32, ≥64	≤8	16	≥32
Ceftazidime	≤1, 2, 4, 8, 16, 32, ≥64	≤4	8	≥16
Ertapenem[d]	≤0.002 to ≥32	≤0.5	1	≥2
Meropenem	≤0.25, 0.5, 1, 2, 4, 8, ≥16	≤1	2	≥4
Gentamicin	≤1, 2, 4, 8, ≥16	≤4	8	≥16
Tobramycin	≤1, 2, 4, 8, ≥16	≤4	8	≥16
Amikacin	≤2, 4, 8, 16, 32, ≥64	≤16	32	≥64
Ciprofloxacin	≤0.25, 0.5, 1, 2, ≥4	≤1	2	≥4
Norfloxacin	≤0.5, 1, 2, 4, 8, ≥16	≤4	8	≥16
Nitrofurantoin	≤16, 32, 64, 128, 256, ≥512	≤32	64	≥128
Nalidixic Acid	≤2, 4, 8, 16, ≥32	≤16	-	≥32
Trimethoprim/sulphamethoxazole	≤1/19, 2/38, 4/76, 8/152, ≥16/304	≤2/38	-	≥4/76
Trimethoprim	≤0.5, 1, 2, 4, 8, ≥16	≤8	-	≥16

[a] The breakpoints selected to determine resistance are described in Performance Standards for Antimicrobial Susceptibility Testing: Twentieth Information Supplement, CLSI document M100-S22, January 2012.
[b] Although included in the Vitek card, results were supressed due to a global recall by BioMérieux
[c] For analysis, breakpoints of ≤4, ≥8 were appied due to the MIC range available on the Vitek card, recognising that the January 2011 breakpoint is actually susceptible ≤ 2 mg/L
[d] Ertapenem MICs performed using Etest strips (BioMérieux).

4.4 QUALITY CONTROL

E. coli ATCC 25922 and *E. coli* ATCC 35218 were the quality control strains for this survey

5 SOURCE OF ISOLATES

The majority of isolates were from urine. 5.6% of isolates overall were from blood cultures; comprising 4.8% of *E. coli* isolates, 7.3% of *Klebsiella* and 8.2% of *Enterobacter* species. Other sites of isolation reflect the high incidence of these species in nosocomial and pre- and post-operative surgical infections.

Table 5. Source of Isolates

Source	*E. coli*		Enterobacter		Klebsiella		Total	
Urine	1448	79.3%	118	43.9%	317	59.0%	1883	71.5%
Respiratory	92	5.0%	66	24.5%	91	16.9%	249	9.5%
Blood	87	4.8%	22	8.2%	39	7.3%	148	5.6%
Skin & soft tissue	81	4.4%	26	9.7%	40	7.4%	147	5.6%
Other	50	2.7%	16	5.9%	22	4.1%	88	3.3%
Intra-abdominal	47	2.6%	8	3.0%	18	3.4%	73	2.8%
Bone & Joint	10	0.5%	6	2.2%	3	0.6%	19	0.7%
Intravascular line	4	0.2%	4	1.5%	6	1.1%	14	0.5%
Sterile site	8	0.4%	3	1.1%	1	0.2%	12	0.5%
Total	1827		269		537		2633	

6 SUSCEPTIBILITY TESTING RESULTS

Overall percentages of resistance or non-susceptibility are shown in Section 6.1 and the Appendix. Appendix 1 shows the details of percentages susceptible, intermediate and resistant for blood culture isolates and isolates from other specimen sources for each antibiotic. For some antibiotics, the concentration range tested did not distinguish between intermediate susceptibility (I) and resistant (R), and the term non-susceptible (NS) was used to describe these strains.

6.1 PERCENTAGES RESISTANT/NON-SUSCEPTIBLE

Table 6. Ampicillin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%I	0.6%	1.3%	0.0%	1.3%	1.1%	0.9%
	%R	55.0%	50.5%	52.1%	48.0%	43.9%	50.5%

Comments: Resistance to ampicillin is intrinsic in *Klebsiella* and *Enterobacter* species, due to natural ß-lactamases, and hence resistance rates not reported here. Some strains may test as susceptible in vitro, but are generally reported as resistant

Table 7. Amoxycillin-clavulanate

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%I	18.4%	15.2%	13.5%	17.1%	13.3%	16.1%
	%R	7.4%	11.1%	9.2%	7.1%	2.5%	7.7%
***Klebsiella* spp.**	%I	7.6%	6.5%	2.0%	12.2%	6.3%	7.6%
	%R	9.0%	5.8%	2.0%	8.9%	6.3%	7.1%
K. pneumoniae	%I	9.7%	8.0%	0.0%	16.7%	1.8%	8.8%
K. pneumoniae	%R	7.8%	3.6%	2.9%	10.0%	3.6%	6.1%
K. oxytoca	%I	2.4%	0.0%	6.7%	0.0%	16.7%	4.4%
K. oxytoca	%R	11.9%	14.8%	0.0%	6.9%	12.5%	10.2%

Comments: Intermediate susceptibility or resistance to amoxycillin-clavulanate is intrinsic in *Enterobacter* species, due to natural ß-lactamases, and hence resistance rates not reported here. Some strains may test as susceptible in vitro, but are generally reported as resistant. Intermediate susceptibility is common in *E. coli* due to hyperproduction of acquired narrow-spectrum ß-lactamases, and in *Klebsiella* species due to higher levels of natural ß-lactamases.

Table 8. Ticarcillin-clavulanate

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	8.0%	10.7%	6.7%	7.3%	5.0%	8.0%
***Enterobacter* spp.**	%R	25.4%	26.1%	26.7%	41.7%	28.2%	29.7%
E. cloacae	%R	38.1%	22.4%	31.8%	45.2%	32.0%	33.9%
E. aerogenes	%R	7.1%	41.2%	14.3%	29.4%	21.4%	21.7%
***Klebsiella* spp.**	%R	13.1%	6.5%	0.0%	13.8%	8.8%	9.7%
K. pneumoniae	%R	12.6%	5.4%	0.0%	16.7%	3.6%	9.1%
K. oxytoca	%R	14.3%	11.1%	0.0%	6.9%	20.8%	11.7%

Comments: Resistance to ticarcillin-clavulanate in *E. coli* and *Klebsiella* species may indicate the presence of acquired plasmid-borne AmpC ß-lactamases.

Table 9. Piperacillin-tazobactam

Resistance to piperacillin-tazobactam was not available for this survey due to a global recall from BioMerieux.

Table 10. Cefazolin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	24.3%	23.8%	23.9%	21.3%	16.5%	22.3%
***Enterobacter* spp.**	%R	85.9%	98.6%	100%	93.3%	74.4%	90.7%
E. cloacae	%R	90.5%	100%	100%	95.2%	80.0%	93.9%
E. aerogenes	%R	78.6%	94.1%	100%	88.2%	64.3%	83.1%
***Klebsiella* spp.**	%R	37.2%	26.6%	24.0%	33.3%	28.8%	31.1%
K. pneumoniae	%R	24.3%	14.3%	5.7%	27.8%	8.9%	18.4%
K. oxytoca	%R	69.0%	77.8%	66.7%	55.2%	75.0%	68.6%

Comments:
Interpretation based on MIC range available on Vitek card, which currently do not match those of the CLSI breakpoints first published in 2011.
Resistance to cefazolin, representative of first generation cephalosporins, is common in *E. coli* and *Klebsiella* species. *Enterobacter* species are intrinsically resistant due to natural ß-lactamases.

Table 11. Cefoxitin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	4.8%	5.4%	5.5%	5.5%	2.5%	4.8%
***Klebsiella* spp.**	%R	4.8%	2.2%	2.0%	4.1%	5.0%	3.7%
K. pneumoniae	%R	5.8%	1.8%	2.9%	5.6%	5.4%	4.3%
K. oxytoca	%R	2.4%	3.7%	0.0%	0.0%	4.2%	2.2%

Comments:
Cefoxitin is tested solely for the purpose of screening for potential plasmid-borne AmpC β-lactamases in *E. coli* and *Klebsiella* spp.. Because *Enterobacter* species have an intrinsic AmpC β-lactamase, they will test as Resistant or Intermediate

Table 12. Ceftriaxone

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%NS	13.0%	10.1%	8.6%	7.9%	5.0%	9.6%
***Enterobacter* spp.**	%NS	36.6%	37.7%	36.7%	53.3%	33.3%	40.1%
E. cloacae	%NS	45.2%	36.7%	36.4%	57.1%	36.0%	43.3%
E. aerogenes	%NS	25.0%	41.2%	42.9%	41.2%	28.6%	33.7%
***Klebsiella* spp.**	%NS	17.2%	10.1%	6.0%	13.8%	2.5%	11.4%
K. pneumoniae	%NS	19.4%	8.9%	5.7%	16.7%	1.8%	12.1%
K. oxytoca	%NS	11.9%	14.8%	6.7%	6.9%	4.2%	9.5%

Comments: In *E. coli* and *Klebsiella* species non-susceptibility to ceftriaxone is indicative of extended-spectrum ß-lactamase production. In *Enterobacter* species resistance is indicative of stable de-repression of natural chromosomal cephalosporinase.

Table 13. Ceftazidime

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%NS	8.6%	5.1%	4.9%	6.0%	1.8%	5.8%
***Enterobacter* spp.**	%NS	32.4%	34.8%	30.0%	50.0%	30.8%	36.4%
E. cloacae	%NS	42.9%	34.7%	31.8%	54.8%	32.0%	40.6%
E. aerogenes	%NS	17.9%	41.2%	28.6%	35.3%	28.6%	28.9%
***Klebsiella* spp.**	%NS	12.4%	7.9%	6.0%	8.9%	1.3%	8.2%
K. pneumoniae	%NS	16.5%	8.0%	5.7%	11.1%	1.8%	9.8%
K. oxytoca	%NS	2.4%	7.4%	6.7%	3.4%	0.0%	3.6%

Comments: In *E. coli* and *Klebsiella* species non-susceptibility to ceftazidime is indicative of extended-spectrum ß-lactamase production. In *Enterobacter* species resistance is indicative of stable de-repression of natural chromosomal cephalosporinase.

Table 14. Cefepime

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%NS	3.7%	0.6%	0.6%	1.6%	1.1%	1.8%
***Enterobacter* spp.**	%NS	0.0%	1.4%	6.7%	8.3%	2.6%	3.3%
E. cloacae	%NS	0.0%	2.0%	9.1%	9.5%	4.0%	4.4%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Klebsiella* spp.**	%NS	4.1%	1.4%	0.0%	0.8%	0.0%	1.7%
K. pneumoniae	%NS	5.8%	1.8%	0.0%	1.1%	0.0%	2.3%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Comments: In *E. coli* and *Klebsiella* species non-susceptibility to cefepime is suggestive of mixed or hyperproduction of extended-spectrum ß-lactamases. In *Enterobacter* species non-susceptibility is suggestive of the presence of extended-spectrum ß-lactamases.

Table 15. Meropenem

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%NS	0.0%	0.2%	0.0%	0.0%	0.0%	0.1%
***Enterobacter* spp.**	%NS	0.0%	0.0%	0.0%	0.0%	2.6%	0.4%
E. cloacae	%NS	0.0%	0.0%	0.0%	0.0%	4.0%	0.6%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Klebsiella* spp.**	%NS	1.4%	0.0%	0.0%	0.0%	0.0%	0.4%
K. pneumoniae	%NS	1.9%	0.0%	0.0%	0.0%	0.0%	0.5%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Comments: Non-susceptibility in Enterobacteriaceae suggests the presence of carbapenemases.

Table 16. Ertapenem

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%NS	0.0%	0.4%	0.0%	0.3%	0.0%	0.2%
***Enterobacter* spp.**	%NS	12.7%	13.0%	3.3%	15.0%	17.9%	13.0%
E. cloacae	%NS	19.0%	14.3%	4.5%	14.3%	28.0%	16.1%
E. aerogenes	%NS	0.0%	11.8%	0.0%	11.8%	0.0%	4.8%
***Klebsiella* spp.**	%NS	2.1%	0.0%	0.0%	0.0%	1.3%	0.7%
K. pneumoniae	%NS	2.9%	0.0%	0.0%	0.0%	1.8%	1.0%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Comments: Non-susceptibility to ertapenem in *Enterobacter* species is linked in part to stably-derepressed chromosomal AmpC β-lactamase production.

Table 17. Ciprofloxacin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%NS	14.5%	9.2%	9.8%	8.9%	7.9%	10.6%
***Enterobacter* spp.**	%NS	0.0%	1.4%	6.7%	6.7%	7.7%	3.7%
E. cloacae	%NS	0.0%	2.0%	9.1%	7.1%	12.0%	5.0%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Klebsiella* spp.**	%NS	6.2%	5.8%	6.0%	8.9%	2.5%	6.1%
K. pneumoniae	%NS	8.7%	7.1%	8.6%	12.2%	3.6%	8.3%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Comments: Ciprofloxacin non-susceptibility indicates at least mutations in *gyrA*, the gene encoding the target enzyme, DNA gyrase and, and more recently, the possibility of plasmid-mediated quinolone-resistance genes

Table 18. Gentamicin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	11.9%	7.1%	5.5%	7.3%	5.4%	8.2%
***Enterobacter* spp.**	%R	12.7%	7.2%	13.3%	15.0%	2.6%	10.4%
E. cloacae	%R	21.4%	10.2%	18.2%	19.0%	4.0%	15.0%
E. aerogenes	%R	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Klebsiella* spp.**	%R	11.7%	8.6%	4.0%	11.4%	0.0%	8.4%
K. pneumoniae	%R	15.5%	9.8%	2.9%	15.6%	0.0%	10.6%
K. oxytoca	%R	2.4%	3.7%	6.7%	0.0%	0.0%	2.2%

Comments: Gentamicin resistance indicates the presence of at least one of a range of aminoglycoside modifying enzymes.

Table 19. Trimethoprim

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	25.3%	24.2%	19.6%	21.3%	23.4%	23.4%
***Enterobacter* spp.**	%R	19.7%	23.2%	20.0%	18.3%	12.8%	19.3%
E. cloacae	%R	31.0%	30.6%	27.3%	23.8%	20.0%	27.2%
E. aerogenes	%R	3.6%	5.9%	0.0%	0.0%	0.0%	2.4%
***Klebsiella* spp.**	%R	12.4%	15.8%	8.0%	26.8%	3.8%	14.9%
K. pneumoniae	%R	17.5%	18.8%	8.6%	32.2%	5.4%	18.7%
K. oxytoca	%R	0.0%	3.7%	6.7%	13.8%	0.0%	4.4%

Comments: Trimethoprim resistance is the result of mutations in the gene encoding dihydrofolate reductase

6.2 SUMMARY

The following summarizes the resistance issues in the three groups of Enterobacteriaceae, except for extended-spectrum ß-lactamases (Section 6.3.1) and carbapenemases (Section 6.3.2). There are no striking differences between the states.

E. coli

Ampicillin resistance proportions have been moderately high for more than a decade, and approximately stable at around 50%. Amoxycillin-clavulanate intermediate and resistant strains have been around for some time but remain in

relatively stable proportion at around 25%. Percentages of resistance to ticarcillin-clavulanate and piperacillin-tazobactam remain low. Cefazolin maintains modest levels of resistance at around 21%. Ciprofloxacin resistance appears to be increasing slowly despite controlled usage in both the community and in hospitals. Gentamicin resistance remains fairly low despite more three decades of use in hospital practice although is higher. Trimethoprim, especially as cotrimoxazole, use has been high in the community and this is reflected in the resistance percentages in hospitals.

***Klebsiella* species**

Rates of resistance to most β-lactam agents tested have risen since 2009. Resistance to gentamicin is still low but higher than 2009. Surprisingly, resistance to ciprofloxacin and trimethoprim is less common than in *E. coli* but also higher than 2009.

***Enterobacter* species**

Ampicillin, amoxicillin-clavulanate and first-generation cephalosporins are intrinsicially inactive against *Enterobacter* species. Resistance to gentamicin is similar to that seen in *E. coli*. Levels of resistance to ciprofloxacin and trimethoprim are less than in *E. coli*.

6.3 MAJOR RESISTANCES

6.3.1 ESBLS

Extended-spectrum ß-lactamases are important problem resistances internationally. They have been predominantly a problem in hospital practice, and initially were more common in *Klebsiella* species than in *E. coli*. Recently, two new trends have emerged: the presence of ESBLs in *Enterobacter* species, and the emergence of specific types of ESBLs (so-called CTX-M enzymes). ESBLs are important as they compromise the efficacy of third-generation cephalosporins which have been such a useful therapeutic alternative in hospital practice. Outbreaks of ESBL producing *Klebsiella* species and *E. coli* have led some hospitals in Australia to severely restrict or abandon third-generation cephalosporin use. ESBLs, particularly those of the CTX-M type, are starting to emerge in community isolates of *E. coli*.

Most ESBL-producing strains will be captured/recognised using the new CLSI ceftriaxone “susceptible” breakpoints of 1 mg/L. The “susceptible”breakpoint of 4 mg/L for ceftazidime is less sensitive for ESBL detection, but an MIC > 1mg/L (which is present on the Vitek 2 card) is more sensitive. Isolates with either ceftriaxone or ceftazidime MICs above 1 mg/L were selected for ESBL phenotypic confirmation and molecular testing.

Neither ceftriaxone nor ceftazidime testing will identify ESBL production in *Enterobacter* species because of their intrinsic chromosomal AmpC β-lactamase. In that species, cefepime at 1 mg/L is suggestive that an isolate of this genus harbours an ESBL. Isolates with a cefepime MIC > 1mg/L were selected for ESBL phenotypic confirmation and molecular testing.

Molecular testing involved multiplex screening for TEM, SHV, CTX-M and plasmid-borne AmpC genes. TEM screening does not accurately discriminiate between TEM-1/2 genes, which encode narrow-spectrum β-lactamases, and TEM genes with higher numbers that encode ESBLs. Similarly, SHV screening does not discriminate between SHV-1/11, which are narrow-spectrum β-lactamases, and SHV genes the encode ESBLs. SHV-1 is the dominant natural chromosomal enzyme of *K. pneumoniae* leading to natural ampicillin/amoxycillin resistance. Therefore, *E. coli* isolates containing only TEM genes and *Klebsiella* species containing only SHV genes have not been classified as carrying an ESBL. All CTX-M genes encode ESBLs, as do plasmid-borne AmpC genes effectively.

Table 20. Presumptive and Confirmed Extended-spectrum β-lactamase Production

Species	NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
Escherichia coli	72	55	18	33	15	193
Ceftriaxone > 1 mg/L	13.0%	10.1%	8.6%	7.9%	5.0%	9.6%
Ceftazidime > 1 mg/L	10.8%	7.3%	9.8%	7.9%	3.2%	8.0%
Either of above	13.4%	11.8%	11.0%	8.7%	5.4%	10.6%
Confirmed						
any ESBL (No. received)	69/72	47/51	14/18	29/33	14/15	173/189
SHV	1	2	1			4
CTX-M types	56	29	11	21	11	128
plasmid-borne AmpC	16	17	2	8	3	46
Klebsiella pneumoniae	22	11	2	15	3	53
Ceftriaxone > 1 mg/L	19.4%	8.9%	5.7%	16.7%	1.8%	12.1%
Ceftazidime > 1 mg/L	20.4%	8.9%	5.7%	15.6%	5.4%	12.6%
Either of above	21.4%	9.8%	5.7%	16.7%	5.4%	13.4%
Confirmed						
any ESBL (No. received)	20/22	11/11	1/2	15/15	1/3	48/53
TEM	14	8	1	13	0	36
CTX-M types	16	7	0	12	0	35
plasmid-borne AmpC	0	2	1	1	1	5
Klebsiella oxytoca	5	4	1	2	1	13
Ceftriaxone > 1 mg/L	11.9%	14.8%	6.7%	6.9%	4.2%	9.5%
Ceftazidime > 1 mg/L	2.4%	7.4%	6.7%	3.4%	0.0%	3.6%
Either of above	11.9%	14.8%	6.7%	6.9%	4.2%	9.5%
Confirmed						
any ESBL (No. received)	1/5	2/4	1/1	1/2	0/1	5/13
TEM	1	1	1	0	0	3
SHV	0	1	1	1	0	3
CTX-M types	0	0	0	0	0	0
plasmid-borne AmpC	0	1	0	0	0	1
***Enterobacter* species**						
Confirmed						
any ESBL (No. received)	10/24	7/22	3/7	11/27	1/11	32/91
CTX-M types	1	2	2	6	0	11
TEM	10	5	3	7	1	26
SHV	7	4	0	6	0	17

* Strains may possess more than one type of ESBL gene

Based on the tests performed in this study, ESBLs appear most common in *Klebsiella* species aloth the difference between those species and *E. coli* has narrowed since 2009. For the *Enterobacter* species 11.9% of isolates contained an ESBL. Overall, there appears to be a substantial increase in CTX-M producing strains compared to 2009.

Many of the *K. oxytoca* isolates with an ESBL phenotype were hyperproducers of K1 β-lactamase, the natural chromosomal enzyme in this species, rather than ESBL producers. Hyperproducers of K1 β-lactamase are consistantly resistant to piperacillin-tazobactam, having borderline resistance to cefepime, but remain susceptible to ceftazidime. This pattern is not typical of a true ESBL producer.

6.3.2 PLASMID-BORNE AmpC β-LACTAMASES

Plasmid-borne AmpC ß-lactamases have recently emerged internationally as a growing Gram-negative resistance problem. They are the result of mobilization of natural chromosomally located genes from common and uncommon species of Enterobacteriaceae onto transmissible plasmids and into the common pathogens. There are currently 6 separate classes. Like ESBLs these enzymes confer resistance to the important third-generation cephalosporins such as ceftriaxone and ceftazidime. Routine phenotypic detection methods have not yet been effectively developed. Nevertheless it is possible to exploit a special feature of these enzymes, their ability to inactivate the cephamycins, represented by cefoxitin. *Enterobacter* species already naturally possess chromosomally-encoded AmpC enzymes.

Table 21. Presumptive plasmid-borne AmpC ß-lactamase Production

Species	NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
Escherichia coli	26	25	9	21	7	88
Cefoxitin ≥ 32 mg/L	4.8%	5.4%	5.5%	5.5%	2.5%	4.8%
***Klebsiella* species**	7	3	1	5	4	20
Cefoxitin ≥ 32 mg/L	4.8%	2.2%	2.0%	4.1%	5.0%	3.7%

The proportions of *E. coli* and *Klebsiella* species with elevated cefoxitin MICs were low. Only 51% of cefoxitin-resistant *E. coli* and 30% of *Klebsiella* spp. that were available for molecular confirmation were confirmed to contain plasmid-borne AmpC; with CIT (n=43), DHA (n=2) and EBC (n=1) in *E. coli,* CIT (n=3), and DHA (n=2) in *K. pneumoniae*, and CIT (n=1) detected in *K. oxytoca*.

6.3.3 CARBAPENEMASES

Acquired carbapenemases, in particular metallo-ß-lactamases, were first described in *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. They are now being seen more commonly among members of the Enterobacteriaceae. Four *K. pneumoniae,* three *E. cloacae* one *K. oxytoca* and in the survey contained $bla_{\text{IMP-4.}}$ Three isolates were non-susceptible using CLSI breakpoints, and all would be sensitive using EUCAST breakpoints. The meropenem MIC range was 1 to 2 mg/L. The $bla_{\text{IMP-4.}}$ producuing strains were detected in three different states, consistent with low slow dissemination of this major form of resistance.

6.4 IMPORTANT CO-RESISTANCES

Strains harbouring extended-spectrum ß-lactamases are much more likely to harbour resistances to unrelated drug classes. The proportion of strains with elevated MICs to ceftriaxone or ceftazidime (>1 mg/L), and confirmed to contain an extended-spectrum ß-lactamase, which were resistant to other drug classes is shown in Table 22:

Table 22. Co-resistance percentages in strains with confirmed ESBLs

Species	Category	Ciprofloxacin	Gentamicin	Trimethoprim*
Escherichia coli (n=176)	%I	1.7%	0.9%	-
	%R	51.1%	42.6%	55.1%
Klebsiella pneumoniae (n=48)	%I	27.1%	0.0%	-
	%R	29.2%	66.7%	79.2%

* There is no intermediate category for trimethoprim

Further detail on co-resistances is contained in Appendix 2.

6.5 MULTI-RESISTANCE

The most problematic Gram-negative pathogens are those with multiple acquired resistances. Although there is no agreed benchmark for the definition of multi-resistance in Enterobacteriaceae, we have chosen acquired resistance to more than 3 agents to define multi-resistance in our survey. For each species, antibiotics were excluded from the count if they were affected by natural resistance mechanisms, so that only true acquired resistances were included. For the purposes of this analysis, resistance included Intermediate susceptibility when the tested range did not go beyond the susceptible category.

Table 23. Multi-resistance in Escherichia coli

		Non-multi-resistant					Multi-resistant										
Region	**Total**	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**%**
NSW/ACT	538	219	107	87	36	83.5%	24	16	21	16	10	1	1					16.5%
QLD/NT	467	207	90	61	46	86.5%	18	16	18	5	6							13.5%
SA	163	75	31	23	12	86.5%	9	4	5	2	2							13.5%
VIC/TAS	381	185	65	57	33	89.2%	12	7	9	5	6	2						10.8%
WA	278	142	47	50	23	94.2%	5	5	2	1	2	1						5.8%
Total	*1827*	*828*	*340*	*278*	*150*	*87.4%*	*68*	*48*	*55*	*29*	*26*	*4*	1					*14.2%*

Antibiotics included: ampicillin, amoxycillin-clavulanate, cefazolin, cefoxitin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
Antibiotics excluded: ticarcillin-clavulanate, piperacillin-tazobactam, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim

Table 24. Multi-resistance in Klebsiella species

		Non-multi-resistant					Multi-resistant										
Region	***Total***	**0**	**1**	**2**	**3**	**%**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**%**
NSW/ACT	145	74	41	2	6	84.8%	6	3	7	5	1						15.2%
QLD/NT	139	78	38	4	6	90.6%	2	5	1	4	1						9.4%
SA	50	25	20	2		94.0%	1	1				1					6.0%
VIC/TAS	123	56	34	9	7	86.2%	11	2	2	1	1						13.8%
WA	80	47	25	5	1	97.5%		1		1							2.5%
Total	*537*	*280*	*158*	*22*	*20*	*89.4%*	*20*	*12*	*10*	*11*	*3*	*1*					*10.6%*

Antibiotics included: amoxycillin-clavulanate, cefazolin, cefoxitin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
Antibiotics excluded: ampicillin, cephalothin, ticarcillin-clavulanate, piperacillin-tazobactam, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim

Table 25. Multi-resistance in Enterobacter species

		Non-multi-resistant					Multi-resistant							
Region	Total	0	1	2	3	%	4	5	6	7	8	9	10	%
NSW/ACT	71	31	16	14	2	88.7%	6	2						11.3%
QLD/NT	69	22	19	16	5	89.9%	6	1						10.1%
SA	30	14	6	1	5	86.7%	1	1	2					13.3%
VIC/TAS	60	20	9	19	6	90.0%	1	3	1	1				10.0%
WA	39	20	6	8	4	97.4%	1							2.6%
Total	*269*	*107*	*56*	*62*	*18*	*90.3%*	*16*	*6*	*3*	1				*9.7%*

Antibiotics included: ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem
Antibiotics excluded: ampicillin, amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, cefoxitin, ticarcillin-clavulanate, tobramycin, norfloxacin, nalidixic acid, sulfamethoxazole-trimethoprim

6.6 LIMITATIONS OF THE STUDY

Although this study is comprehensive in its coverage of Australia, and the methodology follows international standards, there are a small number of limitations to the data and its interpretation.

1. The data are not denominator controlled. There is currently no consensus on an appropriate denominator for such surveys. Institution size, throughput, patient complexity and local antibiotic use patterns very much determine the types of resistance likely to be observed.

2. Every attempt has been made by the participating laboratories to ascertain the clinical significance of isolates; however, the laboratories are dependent on (sometimes very limited) clinical information supplied on request forms. Gathering detailed clinical information sufficient to make a judgment on significance would require much greater resources than were available for this survey.

7 STANDARDS AND INFORMATION RESOURCES

1. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twenty-first informational supplement. M100-S22. CLSI, Wayne, Pa, 2012.

2. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard - Eighth Edition. M07-A8. CLSI, Wayne, Pa, 2009

3. Bell JM, Turnidge JD, Jones RN; SENTRY Asia-Pacific Participants. Prevalence of extended-spectrum beta-lactamase-producing *Enterobacter cloacae* in the Asia-Pacific region: results from the SENTRY Antimicrobial Surveillance Program, 1998 to 2001. *Antimicrob Agents Chemother*. 2003 Dec;47(12):3989-93.

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APPENDIX 1. SUSCEPTIBILITY RESULTS BY REGION

Ampicillin

Genus	Region	Total	%S	%I	%R
Escherichia coli	NSW/ACT	538	44.4%	0.6%	55.0%
	QLD/NT	467	48.2%	1.3%	50.5%
	SA	163	47.9%		52.1%
	VIC/TAS	381	50.7%	1.3%	48.0%
	WA	278	55.0%	1.1%	43.9%
	National	1827	888	17	922
			48.6%	0.9%	50.5%

Amoxycillin-clavulanate

Genus	Region	Total	%S	%I	%R
Escherichia coli	NSW/ACT	538	74.2%	18.4%	7.4%
	QLD/NT	467	73.7%	15.2%	11.1%
	SA	163	77.3%	13.5%	9.2%
	VIC/TAS	381	75.9%	17.1%	7.1%
	WA	278	84.2%	13.3%	2.5%
	National	1827	1392	294	141
			76.2%	16.1%	7.7%
Klebsiella species	NSW/ACT	145	83.4%	7.6%	9.0%
	QLD/NT	139	87.8%	6.5%	5.8%
	SA	50	96.0%	2.0%	2.0%
	VIC/TAS	123	78.9%	12.2%	8.9%
	WA	80	87.5%	6.3%	6.3%
	National	537	458	41	38
			85.3%	7.6%	7.1%

Ticarcillin-clavulanate

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	56.3%	7.0%	25.4%
	QLD/NT	69	62.3%	11.6%	26.1%
	SA	30	66.7%	6.7%	26.7%
	VIC/TAS	60	51.7%	6.7%	41.7%
	WA	39	64.1%	7.7%	28.2%
	National	269	159	22	80
			59.1%	8.2%	29.7%
Escherichia coli	NSW/ACT	538	69.0%	10.6%	8.0%
	QLD/NT	467	81.4%	7.9%	10.7%
	SA	163	84.7%	8.6%	6.7%
	VIC/TAS	381	83.5%	9.2%	7.3%
	WA	278	88.1%	6.8%	5.0%
	National	1827	1452	162	146
			79.5%	8.9%	8.0%
Klebsiella species	NSW/ACT	145	72.4%	4.1%	13.1%
	QLD/NT	139	88.5%	5.0%	6.5%
	SA	50	98.0%	2.0%	0.0%
	VIC/TAS	123	80.5%	5.7%	13.8%
	WA	80	87.5%	3.8%	8.8%
	National	5037	446	24	52
			83.1%	4.5%	9.7%

Piperacillin-tazobactam

Piperacillin-tazobactam susceptibility for *E. coli* not available due to a global recall of the test by BioMérieux

Cefazolin

Genus	Region	Total	%S+I	%R
Enterobacter species	NSW/ACT	71	14.1%	85.9%
	QLD/NT	69	1.4%	98.6%
	SA	30	0.0%	100%
	VIC/TAS	60	6.7%	93.3%
	WA	39	10.3%	74.4%
	National	269	19	244
			7.1%	90.7%
Escherichia coli	NSW/ACT	538	75.7%	24.3%
	QLD/NT	467	76.2%	23.8%
	SA	163	76.1%	23.9%
	VIC/TAS	381	78.7%	21.3%
	WA	278	83.5%	16.5%
	National	1827	1419	408
			77.7%	22.3%
Klebsiella species	NSW/ACT	145	62.8%	37.2%
	QLD/NT	139	73.4%	26.6%
	SA	50	76.0%	24.0%
	VIC/TAS	123	66.7%	33.3%
	WA	80	68.8%	28.8%
	National	537	368	167
			68.5%	31.1%

Cefoxitin

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	8.5%	0.0%	91.5%
	QLD/NT	69	1.4%	0.0%	98.6%
	SA	30	0.0%	3.3%	96.7%
	VIC/TAS	60	8.3%	0.0%	91.7%
	WA	39	5.1%	0.0%	94.9%
	National	269	14	1	254
			5.2%	0.4%	94.4%
Escherichia coli	NSW/ACT	538	93.7%	1.5%	4.8%
	QLD/NT	467	91.9%	2.8%	5.4%
	SA	163	89.6%	4.9%	5.5%
	VIC/TAS	381	92.1%	2.4%	5.5%
	WA	278	96.0%	1.4%	2.5%
	National	1827	1697	42	88
			92.9%	2.3%	4.8%
Klebsiella species	NSW/ACT	145	93.1%	2.1%	4.8%
	QLD/NT	139	96.4%	1.4%	2.2%
	SA	50	98.0%	0.0%	2.0%
	VIC/TAS	123	93.5%	2.4%	4.1%
	WA	80	93.8%	1.3%	5.0%
	National	537	508	9	20
			94.6%	1.7%	3.7%

Ceftriaxone

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	63.4%	1.4%	35.2%
	QLD/NT	69	62.3%	0.0%	37.7%
	SA	30	63.3%	0.0%	36.7%
	VIC/TAS	60	46.7%	1.7%	51.7%
	WA	39	66.7%	2.6%	30.8%
	National	269	161	3	105
			59.9%	1.1%	39.0%
Escherichia coli	NSW/ACT	538	87.0%	0.0%	13.0%
	QLD/NT	467	89.9%	0.0%	10.1%
	SA	163	91.4%	0.0%	8.6%
	VIC/TAS	381	92.1%	0.0%	7.9%
	WA	278	95.0%	0.0%	5.0%
	National	1827	1652	0	175
			90.4%	0.0%	9.6%
Klebsiella species	NSW/ACT	145	82.8%	0.0%	17.2%
	QLD/NT	139	89.9%	0.0%	10.1%
	SA	50	94.0%	0.0%	6.0%
	VIC/TAS	123	86.2%	0.0%	13.8%
	WA	80	97.5%	0.0%	2.5%
	National	537	476	0	61
			88.6%	0.0%	11.4%

Ceftazidime

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	67.6%	1.4%	31.0%
	QLD/NT	69	65.2%	0.0%	34.8%
	SA	30	70.0%	0.0%	30.0%
	VIC/TAS	60	50.0%	3.3%	46.7%
	WA	39	69.2%	2.6%	28.2%
	National	269	171	4	94
			63.6%	1.5%	34.9%
Escherichia coli	NSW/ACT	538	91.4%	0.2%	8.4%
	QLD/NT	467	94.9%	0.0%	5.1%
	SA	163	95.1%	1.2%	3.7%
	VIC/TAS	381	94.0%	0.0%	6.0%
	WA	278	98.2%	0.0%	1.8%
	National	1827	1721	3	103
			94.2%	0.2%	5.6%
Klebsiella species	NSW/ACT	145	87.6%	0.7%	11.7%
	QLD/NT	139	92.1%	0.0%	7.9%
	SA	50	94.0%	0.0%	6.0%
	VIC/TAS	123	91.1%	1.6%	7.3%
	WA	80	98.8%	0.0%	1.3%
	National	537	493	3	41
			91.8%	0.6%	7.6%

Cefepime

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	100%		
	QLD/NT	69	98.6%	0.0%	1.4%
	SA	30	93.3%	0.0%	6.7%
	VIC/TAS	60	91.7%	3.3%	5.0%
	WA	39	97.4%	2.6%	0.0%
	National	269	260	3	6
			96.7%	1.1%	2.2%
Escherichia coli	NSW/ACT	538	96.3%	0.6%	2.8%
	QLD/NT	467	99.4%	0.2%	0.4%
	SA	163	99.4%	0.0%	0.6%
	VIC/TAS	381	98.4%	0.3%	1.3%
	WA	278	98.9%	0.0%	1.1%
	National	1827	1794	7	26
			98.2%	0.4%	1.4%
Klebsiella species	NSW/ACT	145	95.9%	1.4%	2.8%
	QLD/NT	139	98.6%	0.7%	0.7%
	SA	50	100%		
	VIC/TAS	123	99.2%	0.0%	0.8%
	WA	80	100%		
	National	537	528	3	6
			98.3%	0.6%	1.1%

Meropenem

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	100%		
	QLD/NT	69	100%		
	SA	30	100%		
	VIC/TAS	60	100%		
	WA	39	97.4%	2.6%	0.0%
	National	269	239	1	0
			99.6%	0.4%	0.0%
Escherichia coli	NSW/ACT	538	100%		
	QLD/NT	467	99.8%	0.0%	0.2%
	SA	163	100%		
	VIC/TAS	381	100%		
	WA	278	100%		
	National	1827	1826	0	1
			99.9%	0.0%	0.1%
Klebsiella species	NSW/ACT	145	98.6%	1.4%	0.0%
	QLD/NT	139	100%		
	SA	50	100%		
	VIC/TAS	123	100%		
	WA	80	100%		
	National	537	535	2	0
			99.6%	0.4%	0.0%

Ertapenem

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	87.3%	8.5%	4.2%
	QLD/NT	69	87.0%	10.1%	2.9%
	SA	30	96.7%	3.3%	0.0%
	VIC/TAS	60	85.0%	8.3%	6.7%
	WA	39	82.1%	7.7%	10.3%
	National	269	234	22	13
			87.0%	8.2%	4.8%
Escherichia coli	NSW/ACT	538	100%		
	QLD/NT	467	99.6%	0.2%	0.2%
	SA	163	100%		
	VIC/TAS	381	99.7%	0.3%	0.3%
	WA	278	100%		
	National	1827	1824	2	1
			99.8%	0.1%	0.1%
Klebsiella species	NSW/ACT	145	97.9%	0.7%	1.4%
	QLD/NT	139	100%		
	SA	50	100%		
	VIC/TAS	123	100%		
	WA	80	98.8%	0.0%	1.3%
	National	537	533	1	3
			99.3%	0.2%	0.6%

Ciprofloxacin

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	100%		
	QLD/NT	69	98.6%	0.0%	1.4%
	SA	30	93.3%	0.0%	6.7%
	VIC/TAS	60	93.3%	1.7%	5.0%
	WA	39	92.3%	0.0%	7.7%
	National	269	259	1	9
			96.3%	0.4%	3.3%
Escherichia coli	NSW/ACT	538	85.5%	0.9%	13.6%
	QLD/NT	467	90.8%	0.2%	9.0%
	SA	163	90.2%	0.0%	9.8%
	VIC/TAS	381	91.1%	0.5%	8.4%
	WA	278	92.1%	0.4%	7.6%
	National	1827	1634	9	184
			89.4%	0.5%	10.1%
Klebsiella species	NSW/ACT	145	93.8%	2.1%	4.1%
	QLD/NT	139	94.2%	1.4%	4.3%
	SA	50	94.0%	0.0%	6.0%
	VIC/TAS	123	91.1%	7.3%	1.6%
	WA	80	97.5%	0.0%	2.5%
	National	537	504	14	19
			93.9%	2.6%	3.5%

Gentamicin

Genus	Region	Total	%S	%I	%R
Enterobacter species	NSW/ACT	71	87.3%	0.0%	12.7%
	QLD/NT	69	91.3%	1.4%	7.2%
	SA	30	86.7%	0.0%	13.3%
	VIC/TAS	60	85.0%	0.0%	15.0%
	WA	39	97.4%	0.0%	2.6%
	National	269	240	1	28
			89.2%	0.4%	10.4%
Escherichia coli	NSW/ACT	538	87.7%	0.4%	11.9%
	QLD/NT	467	91.9%	1.1%	7.1%
	SA	163	93.3%	1.2%	5.5%
	VIC/TAS	381	92.7%	0.0%	7.3%
	WA	278	94.6%	0.0%	5.4%
	National	1827	1669	9	149
			91.4%	0.5%	8.2%
Klebsiella species	NSW/ACT	145	88.3%	0.0%	11.7%
	QLD/NT	139	91.4%	0.0%	8.6%
	SA	50	94.0%	2.0%	4.0%
	VIC/TAS	123	87.8%	0.8%	11.4%
	WA	80	100%	0.0%	0.0
	National	537	490	2	45
			91.2%	0.4%	8.4%

Trimethoprim

Genus	Region	Total	%S		%R
Enterobacter species	NSW/ACT	71	80.3%		19.7%
	QLD/NT	69	76.8%		23.2%
	SA	30	80.0%		20.0%
	VIC/TAS	60	81.7%		18.3%
	WA	39	87.2%		12.8%
	National	269	217		52
			80.7%		19.3%
Escherichia coli	NSW/ACT	538	74.7%		25.3%
	QLD/NT	467	75.8%		24.2%
	SA	163	80.4%		19.6%
	VIC/TAS	381	78.7%		21.3%
	WA	278	76.6%		23.4%
	National	1827	1400		427
			76.6%		23.4%
Klebsiella species	NSW/ACT	145	87.6%		12.4%
	QLD/NT	139	84.2%		15.8%
	SA	50	92.0%		8.0%
	VIC/TAS	123	73.2%		26.8%
	WA	80	96.3%		3.8%
	National	537	457		80
			85.1%		14.9%

APPENDIX 2. ANTIBIOTIC PROFILES BY FREQUENCY

Enterobacter species (n = 269)

Antibiotic Profile	AUS	QLD/NT	NSW/AC	VIC/TAS	SA	WA
			Region			
CtrCazCpmGenAmkTmpNitCipMer						
Nit	107	30	30	15	12	20
CtrCaz Nit	47	12	10	15	2	8
	35	5	11	10	5	4
TmpNit	16	7	3	2	2	2
CtrCaz	15	3	4	4	3	1
CtrCaz Gen TmpNit	13	4	7		2	
Ctr Nit	7	1	2	2	2	
CtrCaz TmpNit	4	3	1			
CtrCaz Gen Tmp	4	1	1	2		
CtrCazCpmGen TmpNitCip	3			3		
CtrCazCpmGenAmkTmp Cip	2				2	
Tmp	1		1			
Gen TmpNitCip	1	1				
Caz Gen Nit	1			1		
Ctr	1	1				
Ctr TmpNit	1			1		
Ctr TmpNitCip	1					1
Ctr Gen TmpNit	1		1			
CtrCaz Tmp	1			1		
CtrCaz TmpNitCip	1					1
CtrCaz Gen	1			1		
CtrCaz Gen Mer	1					1
CtrCaz Gen TmpNitCip	1			1		
CtrCazCpm	1	1				
CtrCazCpm Nit	1			1		
CtrCazCpm Tmp Cip	1					1
CtrCazCpmGen TmpNit	1			1		

Ctr = ceftriaxone, Caz = ceftazidime, Cpm = cefepime, Gen = gentamicin, Amk = amikacin, Tmp = trimethoprim, Nit = nitrofurantoin, Cip = ciprofloxacin, Mer = meropenem

Escherichia coli (n = 1827

Antibiotic Profile	AUS	QLD/NT	NSW/AC	VIC/TAS	SA	WA
	802	196	212	179	74	141
Amp	224	55	68	41	25	35
AmpAmcCzl	101	28	28	24	9	12
Amp Tmp	95	20	33	16	9	17
AmpAmc	62	18	21	18	1	4
Tmp	39	14	10	6	3	6
AmpAmcCzl Tmp	38	11	8	8	2	9
AmpAmc Tmp	27	11	8	3		5
AmpAmcCzlCfxCtrCaz	26	10	8	5	1	2
Amp Gen Tmp Cip	16	2	9	3		2
Amp Czl	16	3	4	4	1	4
Nit	14	6	5	3		
Amp TmpNit	14		3	7	2	2
Amp Gen Tmp	14	4	3	2	2	3
AmpAmcCzlCfx	13	4	3	3	3	
Amp Cip	10	2	5			3
Amp Nit	10	4	2	2	2	
Amp Tmp Cip	10	4	2	3	1	
Amp Czl Ctr	10	3	5			2
Amp Gen	9	2	3	2	1	1
Amp Czl Ctr Tmp Cip	9	1	4	2	2	
Amp Czl Tmp	8	2	1	1	2	2
AmpAmcCzl CtrCaz Gen Tmp Cip	7	1	4	2		
Tmp Cip	6		2	1		3
AmpAmcCzl Ctr Gen Tmp Cip	6	1	4	1		
AmpAmcCzl CtrCazCpmGen Tmp Cip	6		3	1		2
AmpAmcCzlCfxCtrCaz Tmp	6	2	2	2		
Cip	5		2			3
Amp Czl Ctr Tmp	5	1	1	1		2
AmpAmcCzl Ctr Tmp Cip	5	4	1			
AmpAmcCzl Ctr Gen Tmp	5	1	1	1		2
AmpAmcCzlCfx Tmp	5	3			1	1
TmpNit	4	1	3			
Amp Cfx Cip	4			1		3
Amp Czl Ctr Gen Tmp	4	4				
AmpAmc Gen Cip	4		2	1	1	
AmpAmc Gen Tmp	4		1		1	2
AmpAmcCzl Tmp Cip	4	1	3			
AmpAmcCzl TmpNit	4		2	2		
AmpAmcCzl Gen	4		2		2	
AmpAmcCzlCfxCtr Cip	4	1		1	2	
AmpAmcCzlCfxCtrCazCpmGen TmpNitCip	4		2	2		
Gen	3	2	1			
Gen Tmp	3	1	1	1		
Cfx	3	1		2		
Amp Gen Cip	3	1	2			
Amp Cfx	3	1		1		1

Antibiotic Profile	Region					
AmpAmcCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/AC	VIC/TAS	SA	WA
Amp Cfx Tmp Cip	3	1	1	1		
Amp Czl Cip	3		2		1	
Amp Czl Ctr Cip	3	2			1	
Amp Czl CtrCazCpmGen Cip	3		3			
AmpAmcCzl Nit	3	1	1	1		
AmpAmcCzl Gen Tmp	3		3			
AmpAmcCzl CtrCaz Gen Cip	3	1	2			
AmpAmcCzlCfx Tmp Cip	3	1		1	1	
AmpAmcCzlCfxCtr Tmp Cip	3		1		1	1
AmpAmcCzlCfxCtrCaz Gen Tmp Cip	3	1	1	1		
AmpAmcCzlCfxCtrCazCpm Tmp Cip	3		2			1
TmpNitCip	2	2				
Czl	2	1	1			
Amp Czl TmpNit	2			1		1
Amp Czl Gen Tmp	2	1				1
Amp Czl Caz Gen Tmp	2	2				
Amp Czl Ctr Gen	2		2			
Amp Czl Ctr Gen Cip	2	1	1			
AmpAmc Cip	2	1			1	
AmpAmc Nit	2	1		1		
AmpAmc Tmp Cip	2	1		1		
AmpAmc Cfx Gen Tmp Cip	2	1	1			
AmpAmcCzl Cip	2	1				1
AmpAmcCzl Ctr Gen	2	1		1		
AmpAmcCzl Ctr Gen Cip	2	1				1
AmpAmcCzl Ctr Gen TmpNitCip	2	2				
AmpAmcCzl CtrCaz Tmp Cip	2		2			
AmpAmcCzl CtrCaz Gen Tmp	2		1	1		
AmpAmcCzl CtrCazCpmGen TmpNitCip	2		1	1		
AmpAmcCzlCfx TmpNit	2	2				
AmpAmcCzlCfx Caz	2				2	
AmpAmcCzlCfxCtr Tmp	2			1	1	
AmpAmcCzlCfxCtrCaz Cip	2		2			
AmpAmcCzlCfxCtrCaz NitCip	2	1	1			
AmpAmcCzlCfxCtrCaz TmpNit	2	1			1	
AmpAmcCzlCfxCtrCaz TmpNitCip	2		1	1		
AmpAmcCzlCfxCtrCaz Gen	2		2			
AmpAmcCzlCfxCtrCaz Gen TmpNitCip	2				2	
AmpAmcCzlCfxCtrCazCpmGen Tmp Cip	2	1	1			
NitCip	1		1			
Cfx Tmp Cip	1	1				
Amc	1				1	
Amc Cfx	1		1			
Amc Cfx Nit	1			1		
Amp NitCip	1	1				
Amp TmpNitCip	1		1			
Amp Gen NitCip	1			1		

Antibiotic Profile	Region					
AmpAmcCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/AC	VIC/TAS	SA	WA
Amp Gen TmpNit	1			1		
Amp Gen TmpNitCip	1			1		
Amp Cfx Nit	1		1			
Amp Cfx TmpNitCip	1					1
Amp Cfx Gen Tmp Cip	1	1				
Amp Czl Tmp Cip	1					1
Amp Czl Gen	1			1		
Amp Czl GenAmkTmp	1		1			
Amp Czl Caz	1			1		
Amp Czl Ctr Gen Tmp Cip	1		1			
Amp Czl Ctr CpmGen	1		1			
Amp Czl CtrCaz Cip	1			1		
Amp Czl CtrCazCpm	1		1			
Amp Czl CtrCazCpm Cip	1		1			
Amp CzlCfx Tmp	1			1		
Amp CzlCfx Gen Cip	1			1		
Amp CzlCfxCtr	1			1		
Amp CzlCfxCtrCaz TmpNitCip	1	1				
AmpAmc TmpNit	1			1		
AmpAmc TmpNitCip	1		1			
AmpAmc Gen	1		1			
AmpAmc GenAmkTmp	1		1			
AmpAmc Cfx Nit	1	1				
AmpAmcCzl Gen Cip	1	1				
AmpAmcCzl Gen Tmp Cip	1			1		
AmpAmcCzl GenAmkTmp	1	1				
AmpAmcCzl Ctr Gen TmpNit	1	1				
AmpAmcCzl Ctr Cpm	1		1			
AmpAmcCzl Ctr Cpm AmkTmp Cip	1				1	
AmpAmcCzl CtrCaz Tmp	1		1			
AmpAmcCzl CtrCaz Gen	1	1				
AmpAmcCzl CtrCaz GenAmk Cip	1				1	
AmpAmcCzl CtrCazCpm Cip	1		1			
AmpAmcCzl CtrCazCpm Tmp Cip	1	1				
AmpAmcCzl CtrCazCpm TmpNitCip	1		1			
AmpAmcCzl CtrCazCpmGen Cip	1		1			
AmpAmcCzl CtrCazCpmGen Tmp	1		1			
AmpAmcCzl CtrCazCpmGenAmkTmp Cip	1			1		
AmpAmcCzlCfx Cip	1		1			
AmpAmcCzlCfx Nit	1				1	
AmpAmcCzlCfx Gen Tmp Cip	1		1			
AmpAmcCzlCfx GenAmk Nit	1	1				
AmpAmcCzlCfx Caz Cip	1			1		
AmpAmcCzlCfxCtr Gen Cip	1		1			
AmpAmcCzlCfxCtr Gen Tmp	1					1
AmpAmcCzlCfxCtr CpmGen Tmp Cip	1	1				
AmpAmcCzlCfxCtrCaz Tmp Mer	1	1				

Antibiotic Profile	Region					
AmpAmcCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/AC	VIC/TAS	SA	WA
AmpAmcCzlCfxCtrCaz Tmp Cip	1			1		
AmpAmcCzlCfxCtrCaz Gen Cip	1				1	
AmpAmcCzlCfxCtrCaz Gen NitCip	1			1		
AmpAmcCzlCfxCtrCaz Gen Tmp	1		1			
AmpAmcCzlCfxCtrCazCpm NitCip	1			1		

Amp = ampicillin, Amc = amoxycillin-calvulanate, Czl = cefazolin, Cft = cefoxitin, Ctr = ceftriaxone, Caz = ceftazidime, Cpm = cefepime, Gen = gentamicin, Amk = amikacin, Tmp = trimethoprim, Nit = nitrofurantoin, Cip = ciprofloxacin, Mer = meropenem

Klebsiella species (n = 537)

Antibiotic Profile				Region					
AmcCzlCftCtrCazCpmGenAmkTmpNitCipMer				AUS	QLD/NT	NSW/AC	VIC/TAS	SA	WA
			Nit	216	63	49	41	24	39
				113	29	34	26	11	13
Czl				46	10	16	8	3	9
Czl			Nit	31	9	9	5	5	3
			TmpNit	15	3	4	6	1	1
AmcCzl	CtrCaz	Gen	TmpNitCip	9	3	1	5		
AmcCzl		Gen	TmpNit	8		1	7		
Cfx			Nit	7	1	1	3		2
AmcCzl				5		1			4
AmcCzl			Nit	5	1		1	1	2
			NitCip	4	1	1		2	
Amc			TmpNit	4	2		2		
AmcCzl	Ctr			4	1	3			
AmcCzl	Ctr		Nit	4	1	1	1		1
			Tmp	3	2	1			
AmcCzl	CtrCaz		TmpNitCip	3		2	1		
AmcCzl	CtrCazCpmGen		TmpNitCip	3	2	1			
AmcCzlCfx			Nit	3		1			2
Czl			Tmp	2			2		
Czl			TmpNit	2	2				
Czl	Ctr	Gen	TmpNit	2	1	1			
Czl	CtrCaz		TmpNit	2			2		
AmcCzl	Ctr		TmpNitCip	2			2		
AmcCzl	Ctr	Gen	TmpNitCip	2	1		1		
AmcCzl	CtrCaz	Gen	TmpNit	2	2				
AmcCzlCfxCtrCaz			TmpNit	2	1		1		
AmcCzlCfxCtrCaz		Gen		2		2			
AmcCzlCfxCtrCaz		Gen	TmpNitCip	2		1		1	
-				1					1
-			Nit	1					1
		Gen	TmpNit	1			1		
Cfx			NitCip	1			1		
Czl	Ctr		Nit	1			1		
Czl	Ctr		Tmp	1		1			
Czl	Ctr		TmpNitCip	1					1
Czl	Ctr	Gen	TmpNitCip	1		1			
Czl	CtrCaz	Gen	Nit	1		1			
Czl	CtrCaz	Gen	Tmp	1				1	
Czl	CtrCaz	Gen	TmpNit	1				1	
Czl	CtrCazCpmGen		Nit	1		1			
CzlCfx			Nit	1			1		
CzlCfxCtrCaz		Gen	Tmp	1	1				
CzlCfxCtrCazCpm			TmpNit	1		1			
Amc				1		1			
Amc			Nit	1			1		
Amc			Tmp	1			1		
Amc		Gen	Tmp	1	1				

Antibiotic Profile	Region					
AmcCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/AC	VIC/TAS	SA	WA
AmcCzl NitCip	1		1			
AmcCzl CtrCaz TmpNit	1			1		
AmcCzl CtrCaz Gen Nit	1		1			
AmcCzl CtrCaz Gen Tmp	1		1			
AmcCzl CtrCazCpm Nit	1		1			
AmcCzl CtrCazCpmGen TmpNit	1		1			
AmcCzlCfx Caz TmpNitCip	1					1
AmcCzlCfx Caz Gen TmpNitCip	1	1				
AmcCzlCfxCtr Nit	1			1		
AmcCzlCfxCtrCaz Nit	1	1				
AmcCzlCfxCtrCaz Gen Nit Mer	1		1			
AmcCzlCfxCtrCaz Gen NitCipMer	1		1			
AmcCzlCfxCtrCaz Gen TmpNit	1		1			
AmcCzlCfxCtrCazCpmGen Nit	1		1			
AmcCzlCfxCtrCazCpmGen TmpNitCip	1			1		

Amp = ampicillin, Ptz = piperacillin-tazobactam, Czl = cefazolin, Cft = cefoxitin, Ctr = ceftriaxone, Caz = ceftazidime, Cpm = cefepime, Gen = gentamicin, Amk = amikacin, Tmp = trimethoprim, Nit = nitrofurantoin, Cip = ciprofloxacin, Mer = meropenem

APPENDIX 3. ESBL PROFILES BY FREQUENCY

TEM molecular screening does not discriminate between TEM-1/2 genes, which encode narrow-spectrum β-lactamases, and TEM genes with higher numbers that encode ESBLs. Similarly, SHV screening does not discriminate between SHV-1/11, which are narrow-spectrum β-lactamases, and SHV genes the encode ESBLs. SHV-1 is the dominant natural chromosomal enzyme of *K. pneumoniae* leading to natural ampicillin/amoxycillin resistance.

ESBL Profile[a]	Region					
TemShvCTXampC	AUS	NSW/ACT	QLD/NT	SA	VIC/TAS	WA
Escherichia coli (n=193)						
Tem - CTX -	63	25	19	4	12	3
- - CTX -	60	27	9	7	9	8
- - - ampC	30	10	12	1	5	2
Tem - - ampC	12	3	4	1	3	1
Tem - - -	8	1	2		4	1
- - - -	8	2	2	4		
TemShv - -	3		2	1		
Tem - CTXampC	3	2	1			
TemShvCTX -	1	1				
- - CTXampC	1	1				
(not received)	4		4			
Klebsiella pneumoniae (n=53)						
TemShvCTX -	26	10	5		11	
TemShv - -	7	2	3		2	
- ShvCTX -	7	5	1		1	
- Shv - -	5	2		1		2
- Shv - ampC	2		1			1
Tem - - -	2	2				
TemShv - ampC	1			1		
- ShvCTXampC	1		1			
- - CTX -	1	1				
- - - ampC	1				1	
Klebsiella oxytoca (n=13)						
- - - -	8	4	2		1	1
TemShv - -	2		1	1		
Tem - - -	1	1			1	
Shv - -	1				1	
- - - ampC	1		1			

[a] Tem = TEM, Shv = SHV, Ctx = CTX-M types, ampC = plasmid-borne AmpC, - = no gene detected

APPENDIX 4. MIC DISTRIBUTIONS

Enterobacter aerogenes

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
ampicillin								5 (6.5)	6 (7.8)	11 (14.3)	19 (24.7)	36 (46.8)				77	28.6%	71.4%
co-amoxyclav								3 (3.6)			9 (10.8)	71 (85.5)				83	3.6%	96.4%
Ticarcillin/clavulanate										46 (59.7)	7 (9.1)	2 (2.6)	4 (5.2)	18 (23.4)		77	68.8%	31.2%
cefazolin									13 (15.9)	1 (1.2)		1 (1.2)	67 (81.7)			82	15.9%	84.1%
cefoxitin									3 (3.6)	1 (1.2)		1 (1.2)	78 (94.0)			83	4.8%	95.2%
ceftriaxone							55 (66.3)		4 (4.8)		16 (19.3)	2 (2.4)	6 (7.2)			83	66.3%	33.7%
ceftazidime							53 (63.9)	3 (3.6)	3 (3.6)	1 (1.2)	8 (9.6)		15 (18.1)			83	71.1%	28.9%
cefepime							81 (97.6)	1 (1.2)	1 (1.2)							83	100%	
gentamicin							82 (98.8)	1 (1.2)								83	100%	
tobramycin							83 (100)									83	100%	
amikacin								82 (98.8)		1 (1.2)						83	100%	
nalidixic acid								29 (34.9)	47 (56.6)	4 (4.8)	1 (1.2)	2 (2.4)				83	97.6%	2.4%
ciprofloxacin					82 (98.8)	1 (1.2)										83	100%	
norfloxacin						80 (96.4)	1 (1.2)	2 (2.4)								83	100%	

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
trimethoprim						72	6	2		1	2					83		
						(86.7)	(7.2)	(2.4)		(1.2)	(2.4)						97.6%	2.4%
Trimethoprim/sulfa							80	2			1					83		
							(96.4)	(2.4)			(1.2)						98.8%	1.2%
meropenem					83											83		
					(100)												100%	
ertapenem[b]	14	14	15	10	17	9	2	1	1							83		
	(16.8)	(17.6)	(20.6)	(7.4)	(23.5)	(7.4)	(2.9)	(1.5)	(1.5)								95.2%	4.8%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

[b] Ertapenem MICs performed by Etest strips (BioMérieux), values rounded up to the next double dilution.

Enterobacter cloacae

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
ampicillin								3 (1.7)	1 (0.6)	17 (9.6)	24 (13.5)	133 (74.7)				178	11.8%	88.2%
co-amoxyclav								2 (1.1)	2 (1.1)	6 (3.3)	9 (5.0)	161 (89.4)				180	5.6%	94.4%
Ticarcillin/clavulanate										87 (48.9)	14 (7.9)	6 (3.4)	10 (5.6)	61 (34.3)		178	56.7%	43.3%
cefazolin									6 (3.4)	1 (0.6)	1 (0.6)		167 (95.4)			175	3.4%	96.6%
cefoxitin									8 (4.4)	2 (1.1)	1 (0.6)		169 (93.9)			180	5.6%	94.4%
ceftriaxone							102 (56.7)	3 (1.7)	2 (1.1)	8 (4.4)	11 (6.1)	5 (2.8)	49 (27.2)			180	56.7%	43.3%
ceftazidime							102 (56.7)	2 (1.1)	3 (1.7)	3 (1.7)	13 (7.2)	1 (0.6)	56 (31.1)			180	59.4%	40.6%
cefepime							153 (85.0)	10 (5.6)	7 (3.9)	2 (1.1)	3 (1.7)	1 (0.6)	4 (2.2)			180	95.6%	4.4%
gentamicin							147 (81.7)	1 (0.6)	4 (2.2)	1 (0.6)	27 (15.0)					180	84.4%	15.6%
tobramycin							147 (81.7)	2 (1.1)	3 (1.7)	11 (6.1)	17 (9.4)					180	84.4%	15.6%
amikacin								164 (91.1)	2 (1.1)	1 (0.6)	11 (6.1)	2 (1.1)				180	98.9%	1.1%
nalidixic acid								69 (38.3)	70 (38.9)	7 (3.9)	14 (7.8)	20 (11.1)				180	88.9%	11.1%
ciprofloxacin					156 (86.7)	6 (3.3)	9 (5.0)		9 (5.0)							180	95.0%	5.0%
norfloxacin						150 (83.3)	2 (1.1)	19 (10.6)	1 (0.6)	2 (1.1)	6 (3.3)					180	95.6%	4.4%

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
trimethoprim						91	36	3	1		49					180		
						(50.6)	(20.0)	(1.7)	(0.6)		(27.2)						72.8%	27.2%
Trimethoprim/sulfa							130		2		47					179		
							(72.6)		(1.1)		(26.3)						72.6%	27.4%
meropenem					176	1	2	1								180		
					(97.8)	(0.6)	(1.1)	(0.6)									99.4%	0.6%
ertapenem[b]	31	34	26	17	21	20	20	3	6							178		
	(17.4)	(19.1)	(14.6)	(9.6)	(11.8)	(11.2)	(11.2)	(1.7)	(3.4)								83.7%	16.3%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

[b] Ertapenem MICs performed by Etest strips (BioMérieux), values rounded up to the next double dilution.

Escherichia coli

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
ampicillin								589 (32.2)	202 (11.1)	97 (5.3)	17 (0.9)	922 (50.5)				1827	48.6%	51.4%
co-amoxyclav								564 (30.9)	466 (25.5)	362 (19.8)	294 (16.1)	141 (7.7)				1827	76.2%	23.8%
Ticarcillin/clavulanate										1103 (62.7)	349 (19.8)	73 (4.1)	89 (5.1)	146 (8.3)		1760	82.5%	17.5%
cefazolin									1419 (77.7)	54 (3.0)	84 (4.6)	6 (0.3)	264 (14.4)			1827	77.7%	22.3%
cefoxitin									1629 (89.2)	68 (3.7)	42 (2.3)	29 (1.6)	59 (3.2)			1827	92.9%	7.1%
ceftriaxone							1652 (90.4)			12 (0.7)	25 (1.4)	14 (0.8)	124 (6.8)			1827	90.4%	9.6%
ceftazidime							1680 (92.0)	3 (0.2)	38 (2.1)	3 (0.2)	75 (34.1)		28 (1.5)			1827	94.2%	5.8%
cefepime							1714 (93.8)	51 (2.8)	11 (0.6)	18 (1.0)	7 (0.4)	6 (0.3)	20 (1.1)			1827	98.2%	1.8%
gentamicin							1626 (89.0)	26 (1.4)	17 (0.9)	9 (0.5)	149 (8.2)					1827	91.4%	8.6%
tobramycin							1633 (89.4)	16 (0.9)	17 (0.9)	102 (5.6)	59 (3.2)					1827	91.2%	8.8%
amikacin								1501 (82.2)	236 (12.9)	33 (1.8)	50 (2.7)	4 (0.2)	3 (0.2)			1827	99.6%	0.4%
nalidixic acid								1272 (69.6)	209 (11.4)	33 (1.8)	11 (0.6)	302 (16.5)				1827	83.5%	16.5%
ciprofloxacin					1575 (8623)	42 (2.3)	17 (0.9)	9 (0.5)	184 (10.1)							1827	89.4%	10.6%
norfloxacin						1527 (83.6)	19 (1.0)	92 (5.0)	2 (0.1)	14 (0.8)	173 (9.5)					1827	89.8%	10.2%

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
trimethoprim						1353	21	9	3	14	426					1826		
						(74.1)	(1.2)	(0.5)	(0.2)	(0.8)	(23.3)						76.7%	23.3%
Trimethoprim/sulfa							1378	4	8	1	434					1825		
							(75.5)	(0.2)	(0.4)	(0.1)	(23.8)						75.7%	24.3%
meropenem					1825	1			1							1827		
					(99.9)	(0.1)			(0.1)								99.9%	0.1%
ertapenem[b]	1620	88	34	30	33	7	2			1						1815		
	(89.2)	(4.8)	(1.9)	(1.7)	(1.8)	(0.4)	(0.1)			(0.1)							99.8%	0.2%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

[b] Ertapenem MICs performed by Etest strips (BioMérieux), values rounded up to the next double dilution.

Klebsiella oxytoca

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
ampicillin								3 (2.2)		1 (0.7)	33 (24.1)	100 (73.0)				137	2.9%	97.1%
co-amoxyclav								90 (65.7)	21 (15.3)	6 (4.4)	6 (4.4)	14 (10.2)				137	85.4%	14.6%
Ticarcillin/clavulanate										112 (84.8)	2 (1.5)		2 (1.5)	16 (12.1)		132	86.4%	13.6%
cefazolin									43 (31.4)	36 (26.3)	4 (2.9)		54 (39.4)			137	31.4%	68.6%
cefoxitin									128 (93.4)	4 (2.9)	2 (1.5)		3 (2.2)			137	96.4%	3.6%
ceftriaxone							124 (90.5)		1 (0.7)	6 (4.4)	4 (2.9)	1 (0.7)	1 (0.7)			137	90.5%	9.5%
ceftazidime							132 (96.4)				2 (1.5)		3 (2.2)			137	96.4%	3.6%
cefepime							137 (100)									137	100%	
gentamicin							133 (97.1)			1 (0.7)	3 (2.2)					137	97.1%	2.9%
tobramycin							134 (97.8)			1 (0.7)	2 (1.5)					137	97.8%	2.2%
amikacin								136 (99.3)			1 (0.7)					137	100%	
nalidixic acid								100 (73.0)	27 (19.7)	7 (5.1)	2 (1.5)	1 (0.7)				137	99.3%	0.7%
ciprofloxacin					134 (97.8)	1 (0.7)	2 (1.5)									137	100%	
norfloxacin						135 (98.5)		2 (1.5)								137	100%	

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
trimethoprim						125	6				6					137		
						(91.2)	(4.4)				(4.4)						95.6%	4.4%
Trimethoprim/sulfa							131				6					137		
							(95.6)				(4.4)						95.6%	4.4%
meropenem					136		1									137		
					(99.3)		(0.7)										100%	
ertapenem[b]	119	11		6	1											137		
	(86.9)	(8.0)		(4.4)	(0.7)												100%	

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

[b] Ertapenem MICs performed by Etest strips (BioMérieux), values rounded up to the next double dilution.

Klebsiella pneumoniae

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
ampicillin								6 (1.5)		6 (1.5)	116 (29.3)	268 (67.7)				396	3.0%	97.0%
co-amoxyclav								257 (64.9)	46 (11.6)	34 (8.6)	35 (8.8)	24 (6.1)				396	85.1%	14.9%
Ticarcillin/clavulanate										300 (77.7)	28 (7.3)	10 (2.6)	12 (3.1)	36 (9.3)		386	85.0%	15.0%
cefazolin									321 (81.7)	10 (2.5)	4 (1.0)	1 (0.3)	57 (14.5)			393	81.7%	18.3%
cefoxitin									366 (92.4	6 (1.5)	7 (1.8)	5 (1.3)	12 (3.0)			396	93.9%	6.1%
ceftriaxone							348 (87.9)		2 (0.5)	7 (1.8)	3 (0.8)	4 (1.0)	32 (8.1)			396	87.9%	12.1%
ceftazidime							346 (87.4)		11 (2.8)	3 (0.8)	15 (3.8)		21 (5.3)			396	90.2%	9.8%
cefepime							359 (90.7)	22 (5.6)	2 (0.5)	4 (1.0)	3 (0.8)		6 (1.5)			396	97.7%	2.3%
gentamicin							348 (87.9)	2 (0.5)	3 (0.8)	1 (0.3)	42 (10.6)					396	89.1%	10.9%
tobramycin							342 (86.4)	3 (0.8)	5 (1.3)	22 (5.6)	24 (6.1)					396	88.4%	11.6%
amikacin								379 (95.7)	8 (2.0)	1 (0.3)	8 (2.0)					396	100%	
nalidixic acid								193 (48.7)	118 (29.8)	18 (4.5)	25 (6.3)	42 (10.6)				396	89.4%	10.6%
ciprofloxacin					352 (88.9)	6 (1.5)	5 (1.3)	14 (3.5)	19 (4.8)							396	91.7%	8.3%
norfloxacin						332 (83.8)	5 (1.3)	40 (10.1)		7 (1.8)	12 (3.0)					396	95.2%	4.8%

Drug	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]															Total	%S	%IR
	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256			
trimethoprim						288	9	11	10	4	74					396		
						(72.7)	(2.3)	(2.8)	(2.5)	(1.0)	(18.7)						81.3%	18.7%
Trimethoprim/sulfa							315	10	2	1	68					396		
							(79.5)	(2.5)	(0.5)	(0.3)	(17.2)						82.1%	17.9%
meropenem					390	1	3	2								396		
					(98.5)	(0.3)	(0.8)	(0.5)									99.5%	0.5%
ertapenem[b]	297	44	23	12	10	4	1	2			1					394		
	(75.4)	(11.2)	(5.8)	(3.0)	(2.5)	(1.0)	(0.3)	(0.5)			(0.3)						99.0%	1.0%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

[b] Ertapenem MICs performed by Etest strips (BioMérieux), values rounded up to the next double dilution.