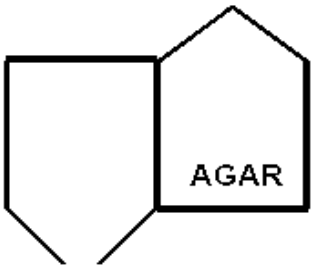

The Australian Group on Antimicrobial Resistance

Gram-negative Survey

2012 Antimicrobial Susceptibility Report

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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 2012 survey focussed on community-onset infections, examining isolates causing urinary tract infections. In all, 29 laboratories covering each state and mainland territory of Australia participated in the 2012 surveillance program. Two thousand and twenty-five *E. coli*, 538 *Klebsiella* species and 239 *Enterobacter* species were tested using a commercial automated method (Vitek 2, BioMérieux). Results were analysed using CLSI breakpoints from January 2013.

Since the first community-onset survey in 2008, the following important changes have been noted: There has been a steady rise in the overall proportion of strains resistant to β-lactam agents in *E. coli*. 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 2008. In *E. coli*, gentamicin resistance has risen from 3.5% to 4.3% and ciprofloxacin resistance has risen from 4.2% to 6.9%. Resistance to carbapenems is still very uncommon in the community. Multi-resistance rates in *E. coli* and *Klebsiella* species have increased from 4.5% and 4.4% respectively in 2008, to 7.6% and 5.1% respectively in 2012.

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 2012 surveillance program were:

1. Determine proportions of resistance to the main therapeutic agents in *E. coli*, *Klebsiella* species, and *Enterobacter* species isolated from outpatients and the community with urinary tract infections
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]

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
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

ß-lactamase	Mainly found in	ß-lactams affected or usual co-resistances	Comments
K1 hyperproduction	*K. oxytoca*	Ampicillin, amoxycillin, piperacillin, first- and second-generation cephalosporins, aztreonam, ceftriaxone > cefotaxime	Natural enzyme selected to hyperproduction
Chromosomal cephalosporinases	ESCaPPM*	Ampicillin, amoxycillin, 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 2012 AGAR survey. Each institution collected up to 70 *E. coli*, 20 *Klebsiella* species, 10 *Enterobacter* species from different outpatient urinary tract infections.

Table 2. Isolates Tested

Region	Number of Institutions	*E. coli*	*Enterobacter* species	*Klebsiella* species	Total
Australian Capital Territory (ACT)	1	70	8	20	98
New South Wales (NSW)	7	490	53	135	678
Northern Territory (NT)	1	70	10	20	100
Queensland (QLD)	6	418	57	119	594

South Australia (SA)	3	210	25	54	289
Tasmania (TAS)	2	140	5	14	159
Victoria (VIC)	5	351	48	99	498
Western Australia (WA)	4	276	33	77	386
Total	**29**	**2,025**	**239**	**538**	**2,802**

4.1 PARTICIPITATING INSTITUTIONS

ACT (1)

The Canberra Hospital

NSW (7)

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

NT (1)

Royal Darwin Hospital

QLD (6)

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

SA (3)

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

TAS (2)

Launceston General Hospital
Royal Hobart Hospital

VIC (5)

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

WA (4)

PathWest, Fremantle Hospital
PathWest, QEII Medical Centre
PathWest, Royal Perth Hospital
St John of God Pathology

4.2 METHODS

4.2.1 SPECIES IDENTIFICATION

Isolates were identified by one of the following methods: Vitek®, Phoenix™ Automated Microbiology System, Microbact, ATB®, or agar replication. In addition, some *E. coli* isolates were identified using chromogenic agar plus spot indole (DMACA).

4.2.2 SPECIES INCLUDED IN STUDY

Table 3. Species included

Group	Organism		Total
E. coli	*E. coli*		2,025
Klebsiella	*K. pneumoniae*		434
	K. oxytoca		101
	K. pneumoniae subsp *ozaenae*		3
		Total	538
Enterobacter	*E. cloacae*		128
	E. aerogenes		107
	E. asburiae		2
	E. gergoviae		1
	Enterobacter not speciated.		1
		Total	239

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-N246 cards were utilized by all participants throughout the survey period. The CLSI breakpoints from Janurary 2013 have been employed in the analysis

4.3.2 ANTIBIOTICS TESTED

Table 4. Antimicrobials Tested

Antimicrobial Agent	AST N246 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	≤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[b]	≤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
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
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-S23, January 2013

[b] For analysis, breakpoints of ≤4 mg/L for susceptible and ≥8 mg/L for resistant were applied due to the MIC range available on the Vitek card, recognising that the January 2013 breakpoint is actually susceptible ≤ 2 mg/L

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

All isolates were collected from non-hospitalised patients with urinary tract infections, including those presenting to emergency departments, outpatient departments or to community practitioners

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 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 5. Ampicillin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%I	1.4%	0.8%	5.7%	2.2%	2.4%	1.4%	2.8%	1.1%	1.9%
	%R	37.1%	47.3%	55.7%	40.5%	39.5%	32.1%	52.1%	43.1%	44.3%

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 6. Amoxycillin-clavulanate

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%I	7.1%	12.7%	12.9%	8.2%	11.4%	8.6%	15.4%	10.1%	11.3%
	%R	5.7%	6.3%	5.7%	4.1%	4.8%	6.4%	6.6%	3.3%	5.3%
***Klebsiella* spp.**	%I	5.0%	3.7%	0.0%	1.7%	1.9%	0.0%	3.0%	1.3%	2.4%
	%R	0.0%	3.0%	5.0%	0.0%	9.3%	0.0%	8.1%	1.3%	3.5%
K. oxytoca	%I	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.3%	0.0%	1.0%
K. oxytoca	%R	0.0%	3.3%	100%	0.0%	20.0%	0.0%	21.7%	0.0%	9.9%
K. pneumoniae	%I	6.7%	4.8%	0.0%	2.0%	2.6%	0.0%	2.7%	1.4%	2.8%
K. pneumoniae	%R	0.0%	2.9%	0.0%	0.0%	5.1%	0.0%	4.0%	1.4%	2.1%

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.

Table7. Ticarcillin-clavulanate

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	4.3%	7.9%	7.1%	4.8%	5.2%	3.6%	6.3%	4.7%	5.7%
***Enterobacter* spp.**	%R	0.0%	24.2%	30.0%	10.5%	12.0%	40.0%	22.9%	18.2%	17.8%
E. aerogenes	%R	0.0%	28.6%	50.0%	10.0%	20.0%	66.7%	23.8%	10.5%	19.8%
E. cloacae	%R	0.0%	22.2%	16.7%	11.1%	6.7%	0.0%	24.0%	28.6%	16.8%
***Klebsiella* spp.**	%R	0.0%	3.8%	5.0%	0.0%	7.4%	0.0%	9.1%	1.3%	3.7%
K. oxytoca	%R	0.0%	5.9%	100%	0.0%	20.0%	0.0%	26.1%	0.0%	12.5%
K. pneumoniae	%R	0.0%	3.2%	0.0%	0.0%	2.6%	0.0%	4.0%	1.4%	1.8%

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

Table 8. Piperacillin-tazobactam

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	1.4%	2.5%	4.4%	0.5%	2.4%	0.0%	2.3%	0.5%	1.7%
***Enterobacter* spp.**	%R	0.0%	11.5%	0.0%	7.0%	4.0%	100%	16.7%	9.1%	9.8%
E. aerogenes	%R	0.0%	16.0%	0.0%	10.0%	10.0%	100%	14.3%	5.3%	11.4%
E. cloacae	%R	0.0%	7.7%	0.0%	5.6%	0.0%	0.0%	20.0%	14.3%	8.8%
***Klebsiella* spp.**	%R	0.0%	1.5%	5.0%	0.0%	5.6%	0.0%	6.1%	0.0%	2.3%
K. oxytoca	%R	0.0%	3.3%	100%	0.0%	20.0%	0.0%	17.4%	0.0%	9.2%
K. pneumoniae	%R	0.0%	1.0%	0.0%	0.0%	0.0%	0.0%	2.7%	0.0%	0.7%

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

Table 9. Cefazolin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	11.4%	18.4%	14.3%	10.3%	18.1%	11.4%	17.1%	8.7%	14.3%
***Enterobacter* spp.**	%R	100%	81.1%	90.0%	93.0%	88.0%	100%	85.4%	72.7%	85.8%
E. aerogenes	%R	100%	64.0%	75.0%	85.0%	70.0%	100%	76.2%	63.2%	73.8%
E. cloacae	%R	100%	100%	100%	97.2%	100%	100%	92.0%	85.7%	96.1%
***Klebsiella* spp.**	%R	25.0%	23.0%	5.0%	15.1%	25.9%	42.9%	26.3%	8.0%	20.0%
K. oxytoca	%R	60.0%	70.0%	100%	64.7%	80.0%	100%	87.0%	75.0%	75.8%
K. pneumoniae	%R	13.3%	9.5%	0.0%	5.9%	5.1%	20.0%	6.7%	4.3%	6.9%

Comments:
Interpretation based on MIC range available on Vitek card, which currently do not match those of the CLSI breakpoints published in 2013. For this analysis, Susceptible was defined as ≤ 4mg/L, Resistant as ≥8 mg/L (no Intermediate range). 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 10. Cefoxitin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	1.4%	2.2%	1.4%	0.7%	1.9%	0.7%	2.0%	1.1%	1.5%
***Klebsiella* spp.**	%R	0.0%	1.5%	0.0%	1.7%	1.9%	0.0%	0.0%	2.6%	1.3%
K. oxytoca	%R	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%R	0.0%	1.9%	0.0%	1.0%	2.6%	0.0%	0.0%	2.9%	1.4%

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 sometimes intermediate.

Table 11. Ceftriaxone

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	1.4%	6.9%	2.9%	2.6%	3.8%	2.1%	4.6%	4.0%	4.2%
***Enterobacter* spp.**	%NS	12.5%	28.3%	40.0%	12.3%	24.0%	40.0%	33.3%	21.2%	24.3%
E. aerogenes	%NS	0.0%	20.0%	50.0%	10.0%	20.0%	66.7%	33.3%	15.8%	21.5%
E. cloacae	%NS	33.3%	37.0%	33.3%	13.9%	26.7%	0.0%	36.0%	28.6%	27.3%
***Klebsiella* spp.**	%NS	5.0%	6.7%	5.0%	3.4%	7.4%	0.0%	8.1%	0.0%	5.0%
K. oxytoca	%NS	0.0%	3.3%	100%	0.0%	13.3%	0.0%	13.0%	0.0%	6.9%
K. pneumoniae	%NS	6.7%	7.6%	0.0%	4.0%	5.1%	0.0%	6.7%	0.0%	4.6%

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 12. Ceftazidime

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	0.0%	3.1%	2.9%	1.2%	2.4%	0.0%	3.4%	1.8%	2.2%
***Enterobacter* spp.**	%NS	12.5%	22.6%	0.0%	8.8%	20.0%	40.0%	29.2%	18.2%	18.8%
E. aerogenes	%NS	0.0%	20.0%	0.0%	10.0%	20.0%	66.7%	33.3%	10.5%	18.7%
E. cloacae	%NS	33.3%	25.9%	0.0%	8.3%	20.0%	0.0%	28.0%	28.6%	19.5%
***Klebsiella* spp.**	%NS	5.0%	3.7%	0.0%	1.7%	3.7%	0.0%	3.0%	0.0%	2.4%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%NS	6.7%	4.8%	0.0%	2.0%	5.1%	0.0%	4.0%	0.0%	3.0%

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 13. Cefepime

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	0.0%	1.0%	1.4%	0.2%	1.9%	0.0%	0.9%	0.0%	0.7%
***Enterobacter* spp.**	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2.1%	0.0%	0.4%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
E. cloacae	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.0%	0.0%	0.8%
***Klebsiella* spp.**	%NS	0.0%	1.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.4%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%NS	0.0%	1.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.5%

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 14. Meropenem

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Enterobacter* spp.**	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.2%	0.0%	0.8%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
E. cloacae	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	8.0%	0.0%	1.6%
***Klebsiella* spp.**	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

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

Table 15. Ciprofloxacin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	5.7%	10.0%	12.9%	4.1%	4.8%	4.3%	6.6%	8.0%	6.9%
***Enterobacter* spp.**	%NS	12.5%	0.0%	0.0%	0.0%	0.0%	0.0%	2.1%	3.0%	1.3%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.8%	5.3%	1.9%
E. cloacae	%NS	33.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.8%
***Klebsiella* spp.**	%NS	5.0%	3.0%	0.0%	2.5%	3.7%	0.0%	4.0%	1.3%	2.8%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%NS	6.7%	3.8%	0.0%	3.0%	5.1%	0.0%	5.3%	1.4%	3.5%

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

Table 16. Norfloxacin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	5.7%	9.6%	12.9%	3.8%	4.8%	4.3%	6.6%	8.0%	6.8%
***Enterobacter* spp.**	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2.1%	3.0%	0.8%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.8%	5.3%	1.9%
E. cloacae	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Klebsiella* spp.**	%NS	5.0%	1.5%	0.0%	1.7%	3.7%	0.0%	2.0%	1.3%	1.9%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%NS	6.7%	1.9%	0.0%	2.0%	5.1%	0.0%	2.7%	1.4%	2.3%

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

Table 17. Gentamicin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	4.3%	6.5%	7.1%	2.2%	4.3%	0.7%	4.3%	5.1%	4.3%
***Enterobacter* spp.**	%R	0.0%	3.8%	0.0%	0.0%	4.0%	0.0%	6.3%	0.0%	2.5%
E. aerogenes	%R	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
E. cloacae	%R	0.0%	7.4%	0.0%	0.0%	6.7%	0.0%	12.0%	0.0%	4.7%
***Klebsiella* spp.**	%R	5.0%	3.0%	0.0%	2.5%	5.6%	0.0%	2.0%	0.0%	2.4%
K. oxytoca	%R	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%R	6.7%	3.8%	0.0%	3.0%	7.7%	0.0%	2.7%	0.0%	3.0%

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

Table 18. Trimethoprim

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	20.0%	23.5%	30.0%	21.1%	21.9%	12.1%	27.6%	22.1%	22.7%
***Enterobacter* spp.**	%R	12.5%	9.4%	10.0%	10.5%	12.0%	0.0%	16.7%	0.0%	10.0%
E. aerogenes	%R	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	9.5%	0.0%	1.9%
E. cloacae	%R	33.3%	18.5%	16.7%	16.7%	20.0%	0.0%	24.0%	0.0%	17.2%
***Klebsiella* spp.**	%R	10.0%	5.2%	10.0%	8.4%	11.1%	0.0%	12.1%	10.4%	8.7%
K. oxytoca	%R	0.0%	0.0%	0.0%	0.0%	13.3%	0.0%	4.3%	0.0%	3.0%
K. pneumoniae	%R	13.3%	6.7%	10.5%	8.9%	10.3%	0.0%	14.7%	11.4%	9.9%

Comments: Trimethoprim resistance is the result of mutations in the gene encoding dihydrofolate reductase (DHFR) or acquisition of a gene encoding a new low affinity DHFR.

Table 19. Nitrofurantoin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	0.0%	1.8%	2.9%	0.5%	1.4%	0.7%	0.3%	0.7%	1.0%
***Enterobacter* spp.**	%R	0.0%	22.6%	20.0%	31.9%	28.0%	60.0%	22.9%	18.2%	24.5%
E. aerogenes	%R	0.0%	36.0%	50.0%	35.7%	30.0%	100%	33.3%	15.8%	31.7%
E. cloacae	%R	0.0%	11.1%	0.0%	31.3%	26.7%	0.0%	16.0%	21.4%	19.4%
***Klebsiella* spp.**	%R	15.0%	17.8%	15.0%	26.0%	20.4%	7.1%	28.3%	16.9%	21.0%
K. oxytoca	%R	0.0%	0.0%	100%	0.0%	6.7%	0.0%	4.3%	0.0%	3.1%
K. pneumoniae	%R	20.0%	22.9%	10.5%	29.1%	25.6%	10.0%	36.0%	18.6%	25.1%

Comments: Nitrofurantoin resistance in *Klebsiella pneumoniae* is partly attributable to the resistance breakpoint within the wild-type distribution.

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 45%. Amoxycillin-clavulanate intermediate and resistant strains have been around for some time but remain in relatively stable proportion at around 17%. Percentages of resistance to ticarcillin-clavulanate and piperacillin-tazobactam remain low. Cefazolin maintains modest levels of resistance at around 15%. Ciprofloxacin resistance appears to be increasing slowly despite controlled usage in both the community and in hospitals (from 4.2% in 2008, 5.4% in 2010, to 7.0% in 2012). Gentamicin resistance remains fairly low despite more three decades of use in hospital practice although is higher. Trimethoprim use, especially in the combination of co-trimoxazole, has been high in the community and this is reflected in the resistance percentages rising slowly to almost 23% resistance now.

***Klebsiella* species**

Rates of resistance to most β-lactam agents tested have remained low and stable since 2008. There has been slow increase in resistance to ceftriaxone over the four-year period, now at 5.0%. Resistance to gentamicin is still low at <3%. Surprisingly, resistance to ciprofloxacin and trimethoprim is less common than in *E. coli* and appears to be stable.

***Enterobacter* species**

Ampicillin, amoxicillin-clavulanate and first-generation cephalosporins are intrinsicially inactive against *Enterobacter* species. Resistance to gentamicin is low and falling. Levels of resistance to ciprofloxacin and trimethoprim are substantially 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) in *E. coli* strains in the community. The latter is part of a global epidemic. It is unclear what is driving this community expansion of CTX-M ESBLs in Australia, as third-generation cephalosporins are not widely used in that setting. ESBLs are important because they compromise the efficacy of third-generation cephalosporins which have been such a useful therapeutic alternative for infections in patients presenting from the community.

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 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 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 in this report. All CTX-M genes encode ESBLs, as do plasmid-borne AmpC genes effectively.

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

Species	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
Escherichia coli	2	35	2	11	9	3	19	11	92
Ceftriaxone > 1 mg/L	1.4%	6.9%	2.9%	2.6%	3.8%	2.1%	4.6%	4.0%	4.2%
Ceftazidime > 1 mg/L	1.4%	5.9%	2.9%	1.9%	3.8%	2.1%	5.1%	3.3%	3.9%
Either of above	2.9%	7.1%	2.9%	2.6%	4.3%	2.1%	5.4%	4.0%	4.5%
Confirmed									
any ESBL (No. received)	2/2	32/34	2/2	10/11	8/9	3/3	15/19	11/11	83/91
CTX-M types	1	27	2	8	7	2	12	9	68
plasmid-borne AmpC	1	5	0	2	1	1	3	3	16
SHV	0	0	0	0	0	0	2	0	2
Klebsiella pneumoniae	1	8	0	4	2	0	5	1	21
Ceftriaxone > 1 mg/L	6.7%	7.6%		4.0%	5.1%		6.7%	0.0%	4.6%
Ceftazidime > 1 mg/L	6.7%	5.7%		3.0%	5.1%		6.7%	1.4%	4.1%
Either of above	6.7%	7.6%		4.0%	5.1%		6.7%	1.4%	4.8%
Confirmed									
any ESBL (No. received)	1/1	6/8	0	3/4	1/2	0	5/5	1/1	17/21
CTX-M types	1	6	0	2	1		4	0	14
plasmid-borne AmpC	0	0	0	0	0	0	0	1	1
TEM	0	4	0	2	1	0	5	0	12
Klebsiella oxytoca	0	1	1	0	2	0	3	0	7
Ceftriaxone > 1 mg/L		3.3%	100%		13.3%		13.0%		6.9%
Ceftazidime > 1 mg/L		0.0%	0.0%		0.0%		0.0%		0.0%
Either of above		3.3%	100%		13.3%		13.0%		6.9%
Confirmed									
any ESBL (No. received)	0	0/1	0/1	0	0/2	0	0/3	0	0/7
***Enterobacter* species**									
Confirmed									
any ESBL (No. received)	0	1/1	0	1/2	0	0	1/2	0	3/4
CTX-M types		1		1	0		0		2
SHV		1		0	0		1		2
TEM		1		0	0		1		2

* Strains may possess more than one type of ESBL gene

Based on the tests performed in this study, ESBLs were found equally among *K. pneumoniae* (3.9% confirmed) and *E. coli* (4.1% confirmed). For the *Enterobacter* species 1.3% of isolates contained an ESBL. There was a notable presence of CTX-M enzymes in *E. coli.* Sixty-eight of 83 (82%) confirmed ESBLs had CTX-M types; CTX-M group 1 (n=41) and CTX-M group 9 (n=27))

All 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, have 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	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
Escherichia coli	1	11	1	3	4	1	7	3	31
Cefoxitin ≥ 32 mg/L	1.4%	2.2%	1.4%	0.7%	1.9%	0.7%	2.0%	1.1%	1.5%
Klebsiella pneumoniae	0	2	0	2	1	0	0	2	7
Cefoxitin ≥ 32 mg/L	0.0%	1.5%	0.0%	1.7%	1.9%	0.0%	0.0%	2.6%	1.3%

The proportions of *E. coli* and *Klebsiella* species with elevated cefoxitin MICs were low. Only 48% of cefoxitin-resistant *E. coli* and 14% of *K. pneumoniae* that were available for molecular confirmation were confirmed to contain plasmid-borne AmpC; with CIT (n=13), and DHA (n=2) in *E. coli,* DHA (n=1) in *K. pneumoniae*.

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. One *E. cloacae* with meropenem MIC ≥ 16 mg/L contained $bla_{IMP-4.}$ This strain also contained bla_{SHV-12}, qnrA and aac(6')-Ib-cr. One other *E. cloacae* was resistant (MIC= 4 mg/L), but no carbapenemase activity was detected.

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=92)	%I	3.6%	1.2%	-
	%R	51.8%	30.1%	56.6%
Klebsiella pneumoniae (n=28)	%I	23.5%	0.0%	-
	%R	29.4%	47.1%	76.5%

* 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.

Only isolates where the full range of antimicrobial agents were tested are included for multi-drug resistance determination.

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***	***%***
ACT	70	41	12	8	5	94.3%	2	1	1									5.7%
NSW	489	233	91	81	30	89.0%	20	14	9	7	2	1		1				11.0%
NT	68	26	15	13	7	89.7%	5				1	1						10.3%
QLD	406	223	87	58	22	96.1%	5	5	3	3								3.9%
SA	210	114	37	28	13	91.4%	10	3	2	1	1	1						8.6%
TAS	72	49	10	7	2	94.4%	3	1										5.6%
VIC	351	142	82	71	29	92.3%	11	7	5	4								7.7%
WA	205	112	34	38	9	94.1%	6	2	3	1								5.9%
Total	*1871*	*940*	*368*	*304*	*117*	*92.4%*	*62*	*33*	*23*	*16*	*4*	*3*		*1*				*7.6%*

Antibiotics included: ampicillin, amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, cefoxitin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem

Antibiotics excluded: ticarcillin-clavulanate, 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***	***%***
ACT	20	13	5		1	95.0%			1								5.0%
NSW	135	83	39	4	2	94.8%	2	1	2	2							5.2%
NT	20	15	4			95.0%		1									5.0%
QLD	99	60	33	1	1	96.0%	2		1	1							4.0%
SA	54	31	14	2	3	92.6%	1	1	1		1						7.4%
TAS	6	4	2			100%											
VIC	99	45	36	9	1	91.9%	6	1			1						8.1%
WA	75	52	17	5		98.7%	1										1.3%
Total	*508*	*303*	*150*	*21*	*8*	*94.9%*	*12*	*4*	*5*	*3*	2						*5.1%*

Antibiotics included: amoxycillin-clavulanate, piperacillin-tazobactam, cefazolin, cefoxitin, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem

Antibiotics excluded: ampicillin, ticarcillin-clavulanate, 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***	***%***
ACT	8	6	1	1		100%								
NSW	52	29	9	5	5	92.3%	4							7.7%
NT	10	4	5	1		100%								
QLD	47	24	14	5	4	100%								
SA	25	13	8	1	2	96.0%		1						4.0%
TAS	1					0.0%	1							100%
VIC	48	25	7	4	6	87.5%	2	3		1				12.5%
WA	33	21	7	2	3	100%								
Total	*224*	*122*	*51*	*19*	*20*	*94.6%*	*7*	4		*1*				*5.4%*

Antibiotics included: piperacillin-tazobactam, ceftriaxone, ceftazidime, cefepime, gentamicin, amikacin, ciprofloxacin, nitrofurantoin, trimethoprim, meropenem

Antibiotics excluded: ampicillin, amoxycillin-clavulanate, 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-third informational supplement. M100-S23. CLSI, Wayne, Pa, 2013.
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 STATE

Ampicillin

Genus	State	Total	%S	%I	%R
Escherichia coli	ACT	70	61.4%	1.4%	37.1%
	NSW	490	51.8%	0.8%	47.3%
	NT	70	38.6%	5.7%	55.7%
	QLD	417	57.3%	2.2%	40.5%
	SA	210	58.1%	2.4%	39.5%
	TAS	140	66.4%	1.4%	32.1%
	VIC	351	45.0%	2.8%	52.1%
	WA	276	55.8%	1.1%	43.1%
	National	2024	1090	38	896
			53.9%	1.9%	44.3%

Amoxycillin-clavulanate

Genus	State	Total	%S	%I	%R
Escherichia coli	ACT	70	87.1%	7.1%	5.7%
	NSW	490	81.0%	12.7%	6.3%
	NT	70	81.4%	12.9%	5.7%
	QLD	417	87.8%	8.2%	4.1%
	SA	210	83.8%	11.4%	4.8%
	TAS	140	85.0%	8.6%	6.4%
	VIC	351	78.1%	15.4%	6.6%
	WA	276	86.6%	10.1%	3.3%
	National	2024	1689	228	107
			83.4%	11.3%	5.3%
Klebsiella species	ACT	20	95.0%	5.0%	0.0%
	NSW	135	93.3%	3.7%	3.0%
	NT	20	95.0%	0.0%	5.0%
	QLD	119	98.3%	1.7%	0.0%
	SA	54	88.9%	1.9%	9.3%
	TAS	14	100%		
	VIC	99	88.9%	3.0%	8.1%
	WA	77	97.4%	1.3%	1.3%
	National	538	506	13	19
			94.1%	2.4%	3.5%

Ticarcillin-clavulanate

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	87.5%	12.5%	0.0%
	NSW	33	69.7%	6.1%	24.2%
	NT	10	70.0%	0.0%	30.0%
	QLD	57	82.5%	7.0%	10.5%
	SA	25	80.0%	8.0%	12.0%
	TAS	5	60.0%	0.0%	40.0%
	VIC	48	68.8%	8.3%	22.9%
	WA	33	72.7%	9.1%	18.2%
	National	219	164	16	39
			74.9%	7.3%	17.8%
Escherichia coli	ACT	70	87.1%	8.6%	4.3%
	NSW	391	82.4%	9.7%	7.9%
	NT	70	82.9%	10.0%	7.1%
	QLD	418	88.8%	6.5%	4.8%
	SA	210	86.2%	8.6%	5.2%
	TAS	140	87.1%	9.3%	3.6%
	VIC	351	82.1%	11.7%	6.3%
	WA	276	89.5%	5.8%	4.7%
	National	1926	1650	166	110
			85.7%	8.6%	5.7%
Klebsiella species	ACT	20	95.0%	5.0%	0.0%
	NSW	79	92.4%	3.8%	3.8%
	NT	20	95.0%	0.0%	5.0%
	QLD	119	97.5%	2.5%	0.0%
	SA	54	87.0%	5.6%	7.4%
	TAS	14	100%		
	VIC	99	87.9%	3.0%	9.1%
	WA	77	97.4%	1.3%	1.3%
	National	482	450	14	18
			93.4%	2.9%	3.7%

Piperacillin-tazobactam

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	100%		
	NSW	52	78.8%	9.6%	11.5%
	NT	10	80.0%	20.0%	0.0%
	QLD	57	89.5%	3.5%	7.0%
	SA	25	84.0%	12.0%	4.0%
	TAS	1			100.0%
	VIC	48	72.9%	10.4%	16.7%
	WA	33	87.9%	3.0%	9.1%
	National	234	193	18	23
			82.5%	7.7%	9.8%
Escherichia coli	ACT	70	94.3%	4.3%	1.4%
	NSW	489	93.0%	4.5%	2.5%
	NT	68	91.2%	4.4%	4.4%
	QLD	407	95.6%	3.9%	0.5%
	SA	210	95.2%	2.4%	2.4%
	TAS	72	98.6%	1.4%	0.0%
	VIC	351	93.4%	4.3%	2.3%
	WA	206	98.5%	1.0%	0.5%
	National	1873	1774	67	32
			94.7%	3.6%	1.7%
Klebsiella species	ACT	20	100%		
	NSW	135	94.8%	3.7%	1.5%
	NT	20	95.0%		5.0%
	QLD	118	100%		
	SA	54	92.6%	1.9%	5.6%
	TAS	6	83.3%	16.7%	0.0%
	VIC	99	91.9%	2.0%	6.1%
	WA	77	97.4%	2.6%	0.0%
	National	529	506	11	12
			95.7%	2.1%	2.3%

Cefazolin

Genus	Region	Total	%S+I	%R
Enterobacter species	ACT	8	0.0%	100%
	NSW	53	18.9%	81.1%
	NT	10	10.0%	90.0%
	QLD	57	7.0%	93.0%
	SA	25	12.0%	88.0%
	TAS	5	0.0%	100%
	VIC	48	14.6%	85.4%
	WA	33	27.3%	72.7%
	National	239	34	205
			14.2%	85.8
Escherichia coli	ACT	70	88.6%	11.4%
	NSW	490	81.6%	18.4%
	NT	70	85.7%	14.3%
	QLD	418	89.7%	10.3%
	SA	210	81.9%	18.1%
	TAS	140	88.6%	11.4%
	VIC	351	82.9%	17.1%
	WA	275	90.9%	8.7%
	National	2024	1735	289
			85.7%	14.3%
Klebsiella species	ACT	20	75.0%	25.0%
	NSW	135	77.0%	23.0%
	NT	20	95.0%	5.0%
	QLD	119	84.9%	15.1%
	SA	54	74.1%	25.9%
	TAS	14	57.1%	42.9%
	VIC	99	73.7%	26.3%
	WA	75	92.0%	8.0%
	National	536	429	107
			80.0%	20.0%

Cefoxitin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	12.5%	0.0%	87.5%
	NSW	53	7.5%	3.8%	88.7%
	NT	10	0.0%	0.0%	100%
	QLD	57	5.3%	3.5%	91.2%
	SA	25	0.0%	0.0%	100%
	TAS	5	0.0%	0.0%	100%
	VIC	48	10.4%	0.0%	89.6%
	WA	33	18.2%	6.1%	75.8%
	National	239	19	6	214
			7.9%	2.5%	89.5%
Escherichia coli	ACT	70	98.6%	0.0%	1.4%
	NSW	490	94.9%	2.9%	2.2%
	NT	70	91.4%	7.1%	1.4%
	QLD	417	97.6%	1.7%	0.7%
	SA	210	95.7%	2.4%	1.9%
	TAS	140	95.7%	3.6%	0.7%
	VIC	351	95.4%	2.6%	2.0%
	WA	276	97.1%	1.8%	1.1%
	National	2024	1943	50	31
			96.0%	2.5%	1.5%
Klebsiella species	ACT	20	100%		
	NSW	135	97.0%	1.5%	1.5%
	NT	20	100%		
	QLD	119	98.3%	0.0%	1.7%
	SA	54	96.3%	1.9%	1.9%
	TAS	14	100%		
	VIC	99	98.0%	2.0%	0.0%
	WA	77	97.4%	0.0%	2.6%
	National	538	526	5	7
			97.8%	0.9%	1.3%

Ceftriaxone

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	87.5%	0.0%	12.5%
	NSW	53	71.7%	1.9%	26.4%
	NT	10	60.0%	0.0%	40.0%
	QLD	57	87.7%	0.0%	12.3%
	SA	25	76.0%	4.0%	20.0%
	TAS	5	60.0%	0.0%	40.0%
	VIC	48	66.7%	0.0%	33.3%
	WA	33	78.8%	3.0%	18.2%
	National	239	181	3	55
			75.7%	1.3%	23.0%
Escherichia coli	ACT	70	98.6%	0.0%	1.4%
	NSW	490	93.1%	0.0%	6.9%
	NT	70	97.1%	0.0%	2.9%
	QLD	418	97.4%	0.0%	2.6%
	SA	210	96.2%	0.0%	3.8%
	TAS	140	97.9%	0.0%	2.1%
	VIC	351	95.4%	0.0%	4.6%
	WA	276	96.0%	0.0%	4.0%
	National	2025	1939	0	86
			95.8%	0.0%	4.2%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	135	93.3%	0.0%	6.7%
	NT	20	95.0%	0.0%	5.0%
	QLD	119	96.6%	0.0%	3.4%
	SA	54	92.6%	0.0%	7.4%
	TAS	14	100%		
	VIC	99	91.9%	0.0%	8.1%
	WA	77	100%		
	National	538	511	0	27
			95.0%	0.0%	5.0%

Ceftazidime

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	87.5%	0.0%	12.5%
	NSW	53	77.4%	0.0%	22.6%
	NT	10	100%		
	QLD	57	91.2%	1.8%	7.0%
	SA	25	80.0%	4.0%	16.0%
	TAS	5	60.0%	0.0%	40.0%
	VIC	48	70.8%	2.1%	27.1%
	WA	33	81.8%	6.1%	12.1%
	National	239	194	5	40
			81.2%	2.1%	16.7%
Escherichia coli	ACT	70	100%		
	NSW	490	96.9%	0.2%	2.9%
	NT	70	97.1%	0.0%	2.9%
	QLD	418	98.8%	0.0%	1.2%
	SA	210	97.6%	0.0%	2.4%
	TAS	140	100%		
	VIC	351	96.6%	0.0%	3.4%
	WA	276	98.2%	0.4%	1.4%
	National	2025	1981	2	42
			97.8%	0.1%	2.1%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	135	96.3%	0.0%	3.7%
	NT	20	100%		
	QLD	119	98.3%	0.0%	1.7%
	SA	54	96.3%	1.9%	1.9%
	TAS	14	100%		
	VIC	99	97.0%	1.0%	2.0%
	WA	77	100%		
	National	538	525	2	11
			97.6%	0.4%	2.0%

Cefepime

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	100%		
	NSW	53	100%		
	NT	10	100%		
	QLD	57	100%		
	SA	25	100%		
	TAS	5	100%		
	VIC	48	97.9%	0.0%	2.1%
	WA	33	100%		
	National	239	238	0	1
			99.6%	0.0%	0.4%
Escherichia coli	ACT	70	100%		
	NSW	490	99.0%	0.2%	0.8%
	NT	70	98.6%	0.0%	1.4%
	QLD	418	99.8%	0.2%	0.0%
	SA	210	98.1%	0.5%	1.4%
	TAS	140	100%		
	VIC	351	99.1%	0.0%	0.9%
	WA	276	100%		
	National	2025	2011	3	11
			99.3%	0.1%	0.5%
Klebsiella species	ACT	20	100%		
	NSW	135	98.5%	0.0%	1.5%
	NT	20	100%		
	QLD	119	100%		
	SA	54	100%		
	TAS	11	100%		
	VIC	99	100%		
	WA	77	100%		
	National	538	536	0	2
			99.6%	0.0%	0.4%

Meropenem

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	100%		
	NSW	53	100%		
	NT	10	100%		
	QLD	57	100%		
	SA	25	100%		
	TAS	5	100%		
	VIC	48	95.8%	0.0%	4.2%
	WA	33	100%		
	National	239	237	0	2
			99.2%	0.0%	0.8%
Escherichia coli	ACT	70	100%		
	NSW	490	100%		
	NT	70	100%		
	QLD	418	100%		
	SA	210	100%		
	TAS	140	100%		
	VIC	351	100%		
	WA	276	100%		
	National	2025	2025		
			100%		
Klebsiella species	ACT	20	100%		
	NSW	135	100%		
	NT	20	100%		
	QLD	119	100%		
	SA	54	100%		
	TAS	14	100%		
	VIC	99	100%		
	WA	77	100%		
	National	538	538		
			100%		

Ciprofloxacin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	87.5%	12.5%	0.0%
	NSW	53	100%		
	NT	10	100%		
	QLD	57	100%		
	SA	25	100%		
	TAS	5	100%		
	VIC	48	97.9%	0.0%	2.1%
	WA	33	97.0%	0.0%	3.0%
	National	239	236	1	2
			98.7%	0.4%	0.8%
Escherichia coli	ACT	70	94.3%	0.0%	5.7%
	NSW	490	90.0%	0.2%	9.8%
	NT	70	87.1%	0.0%	12.9%
	QLD	418	95.9%	0.2%	3.8%
	SA	210	95.2%	0.5%	4.3%
	TAS	140	95.7%	0.0%	4.3%
	VIC	351	93.4%	0.0%	6.6%
	WA	276	92.0%	0.7%	7.2%
	National	2025	1885	5	135
			93.1%	0.2%	6.7%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	135	97.0%	1.5%	1.5%
	NT	20	100%		
	QLD	119	97.5%	0.8%	1.7%
	SA	54	96.3%	0.0%	3.7%
	TAS	14	100%		
	VIC	99	96.0%	2.0%	2.0%
	WA	77	98.7%	0.0%	1.3%
	National	538	523	5	10
			97.2%	0.9%	1.9%

Norfloxacin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	100%		
	NSW	53	100%		
	NT	10	100%		
	QLD	57	100%		
	SA	25	100%		
	TAS	5	100%		
	VIC	48	97.9%	0.0%	2.1%
	WA	33	97.0%	0.0%	3.0%
	National	239	237	0	2
			99.2%	0.4%	0.8%
Escherichia coli	ACT	70	94.3%	0.0%	5.7%
	NSW	490	90.4%	0.4%	9.2%
	NT	70	87.1%	0.0%	12.9%
	QLD	418	96.2%	0.2%	3.6%
	SA	210	95.2%	0.0%	4.8%
	TAS	140	95.7%	0.0%	4.3%
	VIC	351	93.4%	0.9%	5.7%
	WA	276	92.0%	1.8%	6.2%
	National	2025	1888	11	126
			93.2%	0.5%	6.2%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	135	98.5%	0.7%	0.7%
	NT	20	100%		
	QLD	119	98.3%	0.0%	1.7%
	SA	54	96.3%	1.9%	1.9%
	TAS	14	100%		
	VIC	99	98.0%	0.0%	2.0%
	WA	77	98.7%	0.0%	1.3%
	National	538	528	2	8
			98.1%	0.4%	1.5%

Gentamicin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	100%		
	NSW	53	96.2%	0.0%	3.8%
	NT	10	100%		
	QLD	57	100%		
	SA	25	96.0%	0.0%	4.0%
	TAS	5	100%		
	VIC	48	91.7%	2.1%	6.3%
	WA	33	100%		
	National	239	232	1	6
			97.1%	0.4%	2.5%
Escherichia coli	ACT	70	95.7%	0.0%	4.3%
	NSW	490	93.3%	0.2%	6.5%
	NT	70	92.9%	0.0%	7.1%
	QLD	418	97.6%	0.2%	2.2%
	SA	210	95.7%	0.0%	4.3%
	TAS	140	99.3%	0.0%	0.7%
	VIC	351	95.7%	0.0%	4.3%
	WA	276	94.6%	0.4%	5.1%
	National	2025	1934	3	88
			95.6%	0.1%	4.3%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	135	97.0%	0.0%	3.0%
	NT	20	100%		
	QLD	119	97.5%	0.0%	2.5%
	SA	54	94.4%	0.0%	5.6%
	TAS	14	100%		
	VIC	99	98.0%	0.0%	2.0%
	WA	77	100%		
	National	538	525	0	13
			97.6%	0.0%	2.4%

Trimethoprim

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	87.5%		12.5%
	NSW	53	90.6%		9.4%
	NT	10	90.0%		10.0%
	QLD	57	89.5%		10.5%
	SA	25	88.0%		12.0%
	TAS	5	100%		
	VIC	48	83.3%		16.7%
	WA	33	100%		
	National	239	215		24
			90.0%		10.0%
Escherichia coli	ACT	70	80.0%		20.0%
	NSW	490	76.5%		23.5%
	NT	70	70.0%		30.0%
	QLD	417	78.9%		21.1%
	SA	210	78.1%		21.9%
	TAS	140	87.9%		12.1%
	VIC	351	72.4%		27.6%
	WA	276	77.9%		22.1%
	National	2024	1565		459
			77.3%		22.7%
Klebsiella species	ACT	20	90.0%		10.0%
	NSW	135	94.8%		5.2%
	NT	20	90.0%		10.0%
	QLD	119	91.6%		8.4%
	SA	54	88.9%		11.1%
	TAS	14	100%		
	VIC	99	87.9%		12.1%
	WA	77	89.6%		10.4%
	National	538	491		47
			91.3%		8.7%

Nitrofurantoin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	8	12.5%	87.5%	0.0%
	NSW	53	15.1%	62.3%	22.6%
	NT	10	20.0%	60.0%	20.0%
	QLD	47	14.9%	53.2%	31.9%
	SA	25	16.0%	56.0%	28.0%
	TAS	5	20.0%	20.0%	60.0%
	VIC	48	18.8%	58.3%	22.9%
	WA	33	27.3%	54.5%	18.2%
	National	229	41	132	56
			17.9%	57.6%	24.5%
Escherichia coli	ACT	70	95.7%	4.3%	0.0%
	NSW	490	94.3%	3.9%	1.8%
	NT	70	91.4%	5.7%	2.9%
	QLD	417	93.5%	6.0%	0.5%
	SA	210	92.4%	6.2%	1.4%
	TAS	140	98.6%	0.7%	0.7%
	VIC	351	94.3%	5.4%	0.3%
	WA	276	97.1%	2.2%	0.7%
	National	2024	1914	90	20
			94.6%	4.4%	1.0%
Klebsiella species	ACT	20	45.0%	40.0%	15.0%
	NSW	135	31.1%	51.1%	17.8%
	NT	20	10.0%	75.0%	15.0%
	QLD	100	23.0%	51.0%	26.0%
	SA	54	27.8%	51.9%	20.4%
	TAS	14	42.9%	50.0%	7.1%
	VIC	99	28.3%	43.4%	28.3%
	WA	77	28.6%	54.5%	16.9%
	National	519	147	263	109
			28.3%	50.7%	21.0%

APPENDIX 2. ANTIBIOTIC PROFILES BY FREQUENCY

Only isolates where the full range of antimicrobial agents were tested are included in the profiles

***Enterobacter* species** (n = 224)

Antibiotic Profile	Region								
PtzCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
Nit	126	29	28	5	22		16	21	5
	28	6	7	1	7		2	5	
PtzCtrCaz Nit	23	4	8		8	1	1	1	
TmpNit	10	5	2		1		1		1
PtzCtr Nit	5	1			1		1		2
PtzCtrCaz	5	1					1	3	
CtrCaz Nit	4			1	1			2	
Ctr TmpNit	3	1	1		1				
PtzCtrCaz TmpNit	3		1		1		1		
Ctr	2								2
Ctr Nit	2		2						
CtrCaz	2		1				1		
CtrCaz Gen TmpNit	2				1		1		
PtzCtrCaz Gen TmpNit	2		1		1				
Tmp Cip	1				1				
TmpNitCip	1			1					
Gen Tmp	1				1				
Ctr Cip	1							1	
PtzCtrCaz Nit Mer	1				1				
PtzCtrCaz Gen Nit	1		1						
PtzCtrCazCpmGen TmpNit Mer	1				1				

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

Escherichia coli (n = 1871)

Antibiotic Profile	Region								
AmpAmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
	882	205	221	39	131	49	105	108	24
Amp	242	61	57	10	49	6	24	23	12
Amp Tmp	152	36	32	4	35	2	10	26	7
AmpAmc Czl	58	11	17	2	14	2	6	4	2
AmpAmc	55	9	17		14	2	4	7	2
Tmp	54	11	11	2	15	2	8	4	1
AmpAmcPtzCzl Tmp	34	6	9	1	10	1	5	2	
Nit	32	11	10	1	2		6	2	
AmpAmc Czl Tmp	20	3	5	1	4		4	1	2
AmpAmc Tmp	18	4	2	2	7		2	1	
AmpAmcPtzCzl	18	2	8		5				3
Amp Cip	15		3		6	1	1	2	2
Amp Czl	15		4		3	1	6		1
Amp Gen Tmp	14	2	4		3		2	2	1
Amp Tmp Cip	12	1	4		4			2	1
Amp TmpNit	12	4	3	1	2		2		
AmpAmc CzlCfx	10	1			4	3	2		
Amp Czl Ctr Tmp Cip	9	3	4		1	1			
TmpNit	8	1	2		4		1		
Amp Nit	8	1	2		2	1	1		1
Amp Gen Tmp Cip	8		4		2			1	1
Cip	7	2	3	1				1	
Cfx	7	1	1		4			1	
Amp Gen	5	2	1		1			1	
AmpAmc CzlCfxCtrCaz	5		1		2		1	1	
Amp Gen Cip	4	1	1					2	
Amp Czl Tmp	4		1		1		1	1	
Amp Czl Ctr	4		3				1		
Amp Czl Ctr Cip	4		2	1				1	
AmpAmc Nit	4	2	2						
AmpAmc Czl CtrCazCpmGen Cip	4	1	2		1				
AmpAmcPtz	4		2		1		1		
AmpAmcPtz Tmp	4			1	1			1	1
AmpAmcPtzCzlCfxCtrCaz	4	2	1		1				
Tmp Cip	3	1	1		1				
Cfx Nit	3		1		1		1		
Amp NitCip	3	1	1		1				
Amp Cfx	3	1	1					1	
Amp PtzCzl	3	2		1					
AmpAmcPtzCzl Gen Tmp	3	2	1						
Gen	2	1	1						
Amp Gen TmpNitCip	2			1	1				
Amp Cfx Gen Tmp Cip	2								2
Amp Czl Gen Tmp	2		1				1		
Amp Czl Ctr NitCip	2		1				1		
Amp Czl Ctr Gen Tmp	2		2						
Amp Czl CtrCazCpm Tmp Cip	2		1				1		
Amp CzlCfxCtrCazCpm Tmp Cip	2		1				1		
Amp Ptz	2	1			1				
AmpAmc Cip	2		2						
AmpAmc TmpNit	2	1						1	

Antibiotic Profile	Region								
AmpAmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
AmpAmc Czl Cip	2		1		1				
AmpAmc Czl Nit	2	1			1				
AmpAmc Czl CtrCaz Cip	2		1					1	
AmpAmc Czl CtrCaz Tmp Cip	2		1					1	
AmpAmc CzlCfx Tmp	2	1	1						
AmpAmc CzlCfxCtr	2				1	1			
AmpAmc CzlCfxCtr Gen Tmp	2		1					1	
AmpAmcPtzCzl TmpNit	2		1				1		
AmpAmcPtzCzl CtrCazCpm	2				2				
AmpAmcPtzCzlCfx	2		2						
AmpAmcPtzCzlCfx Tmp Cip	2		1				1		
NitCip	1							1	
TmpNitCip	1								1
Gen Tmp	1		1						
Cfx Tmp	1	1							
Cfx Tmp Cip	1		1						
Amc	1						1		
Amp TmpNitCip	1		1						
Amp Gen NitCip	1	1							
Amp Gen TmpNit	1				1				
Amp Cfx Nit	1				1				
Amp Cfx Tmp	1	1							
Amp Cfx Tmp Cip	1		1						
Amp Cfx TmpNit	1								1
Amp Cfx TmpNitCip	1						1		
Amp Cfx Gen TmpNitCip	1				1				
Amp Czl NitCip	1	1							
Amp Czl Tmp Cip	1						1		
Amp Czl Ctr TmpNit	1	1							
Amp Czl Ctr TmpNitCip	1	1							
Amp Czl Ctr Gen Tmp Cip	1		1						
Amp Czl CtrCaz	1				1				
Amp Czl CtrCaz Tmp Cip	1	1							
Amp Czl CtrCaz Gen Cip	1		1						
Amp Czl CtrCaz Gen Tmp	1		1						
Amp Czl CtrCazCpm	1						1		
Amp CzlCfxCtr Cip	1		1						
Amp CzlCfxCtrCaz Cip	1							1	
Amp CzlCfxCtrCaz Tmp	1		1						
Amp CzlCfxCtrCaz Gen Tmp Cip	1		1						
Amp Ptz Tmp	1		1						
Amp PtzCzlCfxCtrCazCpm Tmp	1		1						
AmpAmc Gen	1		1						
AmpAmc Gen Cip	1						1		
AmpAmc Gen NitCip	1							1	
AmpAmc Gen Tmp	1		1						
AmpAmc Cfx	1	1							
AmpAmc Cfx Gen Cip	1		1						
AmpAmc Cfx Gen Tmp	1						1		
AmpAmc Cfx Gen Tmp Cip	1		1						
AmpAmc Czl Gen Tmp	1						1		
AmpAmc Czl Gen Tmp Cip	1							1	
AmpAmc Czl Ctr	1				1				

Antibiotic Profile	Region								
AmpAmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
AmpAmc Czl Ctr Cip	1							1	
AmpAmc Czl Ctr Gen Cip	1				1				
AmpAmc Czl Ctr Gen Tmp	1		1						
AmpAmc Czl Ctr Gen Tmp Cip	1						1		
AmpAmc Czl CtrCaz Gen	1				1				
AmpAmc Czl CtrCaz Gen TmpNit	1				1				
AmpAmc Czl CtrCaz Gen TmpNitCip	1				1				
AmpAmc Czl CtrCazCpmGen TmpNitCip	1								1
AmpAmc CzlCfx Cip	1				1				
AmpAmc CzlCfx Gen Tmp	1			1					
AmpAmc CzlCfxCtr TmpNit	1		1						
AmpAmc CzlCfxCtr Gen Tmp Cip	1		1						
AmpAmc CzlCfxCtrCaz Gen Tmp	1							1	
AmpAmc CzlCfxCtrCaz Gen TmpNitCip	1		1						
AmpAmcPtz Gen Tmp	1		1						
AmpAmcPtz Cfx TmpNit	1								1
AmpAmcPtzCzl Cip	1		1						
AmpAmcPtzCzl NitCip	1	1							
AmpAmcPtzCzl Tmp Cip	1		1						
AmpAmcPtzCzl Gen Cip	1			1					
AmpAmcPtzCzl Gen Nit	1						1		
AmpAmcPtzCzl Ctr Tmp Cip	1	1							
AmpAmcPtzCzl Ctr Gen Tmp	1		1						
AmpAmcPtzCzl CtrCaz Tmp	1				1				
AmpAmcPtzCzl CtrCaz AmkTmp Cip	1								1
AmpAmcPtzCzl CtrCaz Gen TmpNitCip	1				1				
AmpAmcPtzCzlCfx Tmp	1		1						
AmpAmcPtzCzlCfx TmpNitCip	1		1						
AmpAmcPtzCzlCfxCtrCaz Tmp	1	1							
AmpAmcPtzCzlCfxCtrCaz Gen TmpNitCip	1		1						
AmpAmcPtzCzlCfxCtrCazCpmGen TmpNitCip	1						1		

Amp = ampicillin, Amc = amoxycillin-clavulanate, 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 = 508)

Antibiotic Profile	Region								
AmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
Nit	286	65	73	9	52	3	26	43	15
	87	15	25	5	14	1	9	16	2
Czl	39	6	15	4	9	1	2	2	
Czl Nit	23	4	6		4		7	2	
TmpNit	12	2	1		2			5	2
Tmp	7	2			2		1	2	
Cfx Nit	3		2				1		
Amc Czl CtrCaz TmpNitCip	3		1	1	1				
AmcPtzCzl Ctr	3				2		1		
AmcPtzCzl Ctr Nit	3		1		1				1
Gen TmpNit	2			1			1		
Amc Czl CtrCaz Gen TmpNitCip	2	1	1						
AmcPtz TmpNit	2		1					1	
AmcPtzCzl	2				1		1		
AmcPtzCzl Nit	2				2				
NitCip	1							1	
Tmp Cip	1		1						
TmpNitCip	1				1				
Gen TmpNitCip	1	1							
Cfx TmpNit	1				1				
Czl TmpNit	1				1				
Czl Ctr Nit	1		1						
Czl Ctr TmpNit	1	1							
Czl Ctr Gen Nit	1		1						
Czl CtrCaz TmpNit	1				1				
Czl CtrCaz Gen TmpNitCip	1	1							
CzlCfx	1							1	
CzlCfx Nit	1				1				
CzlCfx TmpNit	1	1							
Ptz	1							1	
Ptz TmpNitCip	1						1		
PtzCzl	1					1			
PtzCzl Nit	1		1						
Amc Nit	1		1						
Amc TmpNit	1						1		
Amc Czl Ctr Gen TmpNit	1				1				
Amc Czl Ctr Gen TmpNitCip	1				1				
Amc Czl CtrCaz Gen Nit	1						1		
Amc CzlCfx Nit	1							1	
Amc CzlCfxCtrCaz Gen TmpNitCip	1						1		
AmcPtz Nit	1				1				
AmcPtzCzl Ctr Tmp	1						1		
AmcPtzCzl Ctr TmpNit	1		1						
AmcPtzCzl CtrCaz TmpNitCip	1				1				
AmcPtzCzl CtrCaz Gen Tmp Cip	1		1						
AmcPtzCzlCfxCtrCazCpm Nit	1		1						
AmcPtzCzlCfxCtrCazCpmGen Nit	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	Total	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Escherichia coli (n = 92)									
- - CTX -	39		17	1	7	3	2	6	3
Tem - CTX -	26	1	10	1	1	4		4	5
- - - ampC	11	1	4		1	1	1	3	
- - - -	6				1	1		4	
Tem - - ampC	4		1		1				2
Tem - - -	2		2						
TemShvCTX -	2							2	
Tem - CTXampC	1								1
(not received)	1		1						
Klebsiella pneumoniae (n = 21)									
TemShvCTX -	9		3		1	1		4	
- ShvCTX -	4	1	2		1				
- - - -	2		1			1			
- Shv - -	2		1		1				
TemShv - -	2				1			1	
- - - ampC	1								1
Tem - CTX -	1		1						
Klebsiella oxytoca (n = 7)									
- - - -	7		1	1		2		3	

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

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								10 (10.4)	5 (5.2)	22 (22.9)	27 (28.1)	32 (33.3)				96	38.5%	61.5%
co-amoxyclav								8 (7.5)	4 (3.7)	1 (0.9)	9 (8.4)	85 (79.4)				107	12.1%	87.9%
ticarcillin/clavulanate										71 (74.0)		1 (1.0)	5 (5.2)	19 (19.8)		96	74.0%	26.0%
piperacillin/tazobactam									75 (71.4)	7 (6.7)	3 (2.9)	2 (1.9)	6 (5.7)	12 (11.4)		105	81.0%	19.0%
cefazolin									28 (26.2)			1 (0.9)	78 (72.9)			107	26.2%	73.8%
cefoxitin									6 (5.6)	1 (0.9)	4 (3.7)	5 (4.7)	91 (85.0)			107	6.5%	93.5%
ceftriaxone							84 (78.5)	1 (0.9)	3 (2.8)		11 (10.3)	3 (2.8)	5 (4.7)			107	78.5%	21.5%
ceftazidime							83 (77.6)	4 (3.7)			6 (5.6)	2 (1.9)	12 (11.2)			107	81.3%	18.7%
cefepime							107 (100)									107	100%	
gentamicin							107 (100)									107	100%	
tobramycin							107 (100)									107	100%	
amikacin								107 (100)								107	100%	
ciprofloxacin					103 (96.3)	1 (0.9)	1 (0.9)		2 (1.9)							107	98.1%	1.9%
norfloxacin						99 (92.5)	2 (1.9)	4 (3.7)			2 (1.9)					107	98.1%	1.9%

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						103 (96.3)		2 (1.9)			2 (1.9)					107	98.1%	1.9%
trimethoprim/sulfa							105 (98.1)	1 (0.9)			1 (0.9)					107	99.1%	0.9%
meropenem					107 (100)											107	100%	

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN246 card; vertical lines indicate CLSI M100-S23 susceptible (blue) and resistant (red) breakpoints.

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 (2.5)	5 (4.2)	14 (11.7)	35 (292)	63 (52.5)				120	18.3%	81.7%
co-amoxyclav								5 (3.9)	4 (3.1)	9 (7.0)	15 (11.7)	95 (74.2)				128	14.1%	85.9%
ticarcillin/clavulanate										77 (64.7)	12 (10.1)	5 (4.2)	5 (4.2)	20 (16.8)		119	74.8%	25.2%
piperacillin/tazobactam									85 (68.0)	11 (8.8)	8 (6.4)	4 (3.2)	6 (4.8)	11 (8.8)		125	83.2%	16.8%
cefazolin									5 (3.9)	1 (0.8)	3 (2.3)	1 (0.8)	118 (92.2)			128	3.9%	96.1%
cefoxitin									6 (4.7)	5 (3.9)	2 (1.6)	4 (3.1)	111 (86.7)			128	8.6%	91.4%
ceftriaxone							93 (72.7)	2 (1.6)	1 (0.8)	6 (4.7)	6 (4.7)	5 (3.9)	15 (11.7)			128	72.7%	27.3%
ceftazidime							97 (75.8)	2 (1.6)	4 (3.1)	5 (3.9)	5 (3.9)		15 (11.7)			128	80.5%	19.5%
cefepime							123 (96.1)	4 (3.1)					1 (0.8)			128	99.2%	0.8%
gentamicin							117 (91.4)	1 (0.8)	3 (2.3)	1 (0.8)	6 (4.7)					128	94.5%	5.5%
tobramycin							118 (92.2)	2 (1.6)	2 (1.6)	4 (3.1)	2 (1.6)					128	95.3%	4.7%
amikacin								125 (97.7)		1 (0.8)	2 (1.6)					128	100%	
ciprofloxacin					125 (97.7)	1 (0.8)	1 (0.8)	1 (0.8)								128	99.2%	0.8%
norfloxacin						121 (94.5)	2 (1.6)	4 (3.1)	1 (0.8)							128	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						101 (78.9)	2 (1.6)	1 (0.8)	1 (0.8)	1 (0.8)	22 (17.2)					128	82.8%	17.2%
trimethoprim/sulfa							107 (83.6)			1 (0.8)	20 (15.6)					128	83.6%	16.4%
meropenem					126 (98.4)				1 (0.8)		1 (0.8)					128	98.4%	1.6%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN246 card; vertical lines indicate CLSI M100-S23 susceptible (blue) and resistant (red) breakpoints.

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								553 (27.3)	314 (15.5)	223 (11.0)	38 (1.9)	896 (44.3)				2024	53.9%	46.1%
co-amoxyclav								706 (34.9)	607 (30.0)	376 (18.6)	228 (11.3)	107 (5.3)				2024	83.4%	16.6%
ticarcillin/clavulanate										1179 (61.2)	471 (24.5)	110 (5.7)	56 (2.9)	110 (5.7)		1926	85.7%	14.3%
piperacillin/tazobactam									1731 (92.4)	32 (1.7)	11 (0.6)	10 (0.5)	57 (3.0)	32 (1.7)		1873	94.7%	5.3%
cefazolin									1735 (85.7)	48 (2.4)	100 (4.9)	8 (0.4)	133 (6.6)			2024	85.7%	14.3%
cefoxitin									1860 (91.9)	83 (4.1)	50 (2.5)	11 (0.5)	20 (1.0)			2024	96.0%	4.0%
ceftriaxone							1939 (95.8)		1 (0.0)	5 (0.2)	8 (0.4)	6 (0.3)	66 (3.3)			2025	95.8%	4.2%
ceftazidime							1947 (96.1)	5 (0.2)	29 (1.4)	2 (0.1)	34 (1.7)		8 (0.4)			2025	97.8%	2.2%
cefepime							1962 (96.9)	35 (1.7)	4 (0.2)	10 (0.5)	3 (0.1)	1 (0.1)	10 (0.5)			2025	99.3%	0.7%
gentamicin							1922 (94.9)	11 (0.5)	1 (0.0)	3 (0.1)	88 (4.3)					2025	95.5%	4.5%
tobramycin							1917 (94.7)	10 (0.5)	4 (0.2)	76 (3.8)	18 (0.9)					2025	95.4%	4.6%
amikacin								1931 (95.4)	75 (3.7)	12 (0.6)	6 (0.3)		1 (0.0)			2025	99.9%	<0.1%
ciprofloxacin					1836 (90.7)	31 (1.5)	18 (0.9)	5 (0.2)	134 (6.6)							2024	93.1%	6.9%
norfloxacin						1776 (87.7)	22 (1.1)	89 (4.4)	1 (0.0)	11 (0.5	126 (6.2)					2025	93.2%	6.8%

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						1549 (76.5)	4 (0.2)	4 (0.2)	4 (0.2)	4 (0.2)	459 (22.7)					2024	77.3%	22.7%
trimethoprim/sulfa							1606 (79.3)	2 (0.1)	2 (0.1)	1 (0.0)	414 (20.4)					2025	79.4%	20.6%
meropenem					2025 (100)											2025	100%	

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN246 card; vertical lines indicate CLSI M100-S23 susceptible (blue) and resistant (red) breakpoints.

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										1 (1.0)	20 (19.8)	80 (79.2)				101	1.0%	99.0%
co-amoxyclav								58 (57.4)	28 (27.7)	4 (4.0)	1 (1.0)	10 (9.9)				101	89.1%	10.9%
ticarcillin/clavulanate										74 (84.1)	3 (3.4)			11 (12.5)		88	87.5%	12.5%
piperacillin/tazobactam									83 (84.7)	1 (1.0)	2 (2.0)	3 (3.1)		9 (9.2)		98	87.8%	12.2%
cefazolin									24 (24.2)	26 (26.3)	15 (15.2)		34 (34.3)			99	24.2%	75.8%
cefoxitin									96 (95.0)	4 (4.0)	1 (1.0)					101	99.0%	1.0%
ceftriaxone							94 (92.2)		1 (1.0)	4 (4.0)	1 (1.0)		1 (1.0)			101	93.1%	6.9%
ceftazidime							101 (100)									101	100%	
cefepime							101 (100)									101	100%	
gentamicin							100 (99.0)	1 (1.0)								101	100%	
tobramycin							101 (100)									101	100%	
amikacin								101 (100)								101	100%	
ciprofloxacin					101 (100)											101	100%	
norfloxacin						100 (99.0)	1 (1.0)									101	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						94 (93.1)	2 (2.0)	1 (1.0)	1 (1.0)		3 (3.0)					101	97.0%	3.0%
trimethoprim/sulfa							98 (97.0)				3 (3.0)					101	97.0%	3.0%
meropenem					101 (100)											101	100%	

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek ASTN246 card; vertical lines indicate CLSI M100-S23 susceptible (blue) and resistant (red) breakpoints.

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								11 (2.5)	1 (0.2)	10 (2.3)	140 (32.3)	272 (62.7)				434	5.1%	94.9%
co-amoxyclav								325 (74.9)	49 (11.3)	39 (9.0)	12 (2.8)	9 (2.1)				434	95.2%	4.8%
ticarcillin/clavulanate										356 (91.0)	14 (3.6)	7 (1.8)	7 (1.8)	7 (1.8)		391	94.6%	5.4%
piperacillin/tazobactam									386 (90.2)	19 (4.4)	12 (2.8)	5 (1.2)	3 (0.7)	3 (0.7)		428	97.4%	2.6%
cefazolin									404 (93.1)	2 (0.5)	4 (0.9)		24 (5.5)			434	93.1%	6.9%
cefoxitin									410 (94.5)	14 (3.2)	4 (0.9)	4 (0.9)	2 (0.5)			434	97.7%	2.3%
ceftriaxone							414 (95.4)		1 (0.2)	4 (0.9)		1 (0.2)	14 (3.2)			434	95.4%	4.6%
ceftazidime							416 (95.9)	2 (0.5)	3 (0.7)	2 (0.5)	7 (1.6)		4 (0.9)			434	97.0%	3.0%
cefepime							421 (97.0)	7 (1.6)	1 (0.2)	3 (0.7)			2 (0.5)			434	99.5%	0.5%
gentamicin							421 (97.0)				13 (3.0)					434	97.0%	3.0%
tobramycin							416 (95.9)	2 (0.5)		7 (1.6)	9 (2.1)					434	96.3%	3.7%
amikacin								427 (98.4)	3 (0.7)	2 (0.5)	2 (0.5)					434	100%	
ciprofloxacin					404 (93.1)	1 (0.2)	14 (3.2)	5 (1.2)	10 (2.3)							434	96.5%	3.5%
norfloxacin						399 (91.9)	2 (0.5)	21 (4.8)	2 (0.5)	2 (0.5)	8 (1.8)					434	97.7%	2.3%

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						382 (88.0)	1 (0.2)	6 (1.4)	1 (0.2)	1 (0.2)	43 (9.9)					434	90.1%	9.9%
trimethoprim/sulfa							394 (90.8)	6 (1.4)			34 (7.8)					434	92.2%	7.8%
meropenem					434 (100)											434	100%	

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