The Australian Group on Antimicrobial Resistance

Gram-negative Survey

Community-Onset Infections

2010 Antimicrobial Susceptibility Report

Prepared by

Professor John Turnidge
SA Pathology (Women's and Children's Hospital)
Adelaide

A/Professor Thomas Gottlieb
Concord Hospital
Sydney

Dr David Mitchell
Westmead Hospital
Sydney

Julie Pearson
PathWest Laboratory Medicine WA, Royal Perth Hospital
Perth

Jan Bell
SA Pathology (Women's and Children's Hospital)
Adelaide

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

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1 TABLE OF CONTENTS

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 2010 survey focussed on community-onset infections, examining isolates from urinary tract infections from patients presenting to outpatient clinics, emergency departments or to community practitioners. In all, 30 laboratories covering each state and mainland territory of Australia participated in the 2010 surveillance program. Two thousand and ninety-two *E. coli*, 578 *Klebsiella* species and 268 *Enterobacter* species were tested using a commercial automated method (Vitek 2, BioMérieux). Results were analysed using CLSI breakpoints from January 2012.

Moderately high levels of resistance to ampicillin (and therefore amoxycillin) were observed in ***E. coli*** (43%), with lower rates for amoxycillin-clavulanate (14.8% intermediate, 6.2% resistant). Non-susceptibility to third-generation cephalosporins is low but appears to be increasing slowly (ceftriaxone 3.2%, ceftazidime 1.9%). In line with international trends among community strains of *E. coli*, most of the strains with extended-spectrum β-lactamase (ESBL) genes harboured genes of the CTX-M type (51/65 = 78%). Moderate levels of resistance were detected to cefazolin (15.2%) and trimethoprim (21.2%). Ciprofloxacin non-susceptibility was found in 5.4% of *E. coli* isolates, higher than that of the other Gram-negative species examined. Ciprofloxacin resistance was found in 60.3% and gentamicin resistance was found in 49.2% of ESBL producing strains. Resistance to ticarcillin-clavulanate, piperacillin-tazobactam, cefepime, and gentamicin were below 5%. No isolates had elevated meropenem MICs but 2 (0.1%) strains had elevated ertapenem MICs. Seven of the 9 strains contained CTX-M-types or plasmid-borne ampC.

Compared to *E. coli*, ***Klebsiella* species** showed slightly higher levels of resistance to cefazolin, ceftriaxone, and piperacillin-tazobactam, but lower rates of resistance to amoxycillin-clavulanate, ticarcicllin-clavulanate, ciprofloxacin, gentamicin, and trimethoprim. ESBLs were present in all 17 presumptively ESBL-positive isolates of *K. pneumoniae*, 12 of which also proved to be of the CTX-M type. Two of three strains of *K. pneumoniae* with elevated meropenem MICs (≥ 0.5 mg/L) harboured $bla_{\text{IMP-4}}$, while two additional strains had elevated ertapenem MICs, but neither harboured a known carbapenemase.

In ***Enterobacter* species** acquired resistance was common to ticarcillin-clavulanate (19.8%), piperacillin-tazobactam (17.2%), ceftriaxone (23.9%), ceftazidime (20.9%) and trimethoprim (12.3%). Rates of resistance to cefepime, ciprofloxacin, and gentamicin were all less than 5%. Five of 12 strains tested for extended-spectrum β-lactamases based on a suspicious phenotype harboured ESBL-encoding genes. Three strains had elevated meropenem MICs (≥ 0.5 mg/L) one of which harboured $bla_{\text{IMP-4}}$, while 11% of strains had elevated ertapenem MICs, which appeared to bear some relationship to stably-derepressed chromosomal AmpC β-lactamase.

There are worrying trends in the emergence of CTX-M-producing *E. coli* and *Klebsiella* species and ciprofloxacin-resistant *E. coli* now presenting in or from the community. Other resistance patterns appear stable. There were no striking differences in resistance rates between the states/territories.

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, have 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 2010 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.

Enterobacter species are predominantly hospital-acquired pathogens. They are intrinsically resistant to aminopenicillins, first and second generation cephalosporins including cefamycins. Hence, they are naturally multi-resistant. They acquire resistance to important Gram-negative agents relatively easily.

3.3 RELEVANCE OF ANTIMICROBIALS TESTED

3.3.1 Β-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
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, amoxycillin, piperacillin, first- and second-generation cephalosporins, aztreonam, ceftriaxone > cefotaxime	Natural enzyme selected to hyperproduction

ß-lactamase	Mainly found in	ß-lactams affected or usual co-resistances	Comments
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 mutations resulting in 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

Thirty institutions from each State and mainland Territories of Australia participated in the Gram-negative 2010 AGAR survey. Each institution collected up to 70 *E. coli*, 20 *Klebsiella* species and 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	10	20	100
New South Wales (NSW)	7	488	64	139	691
Northern Territory (NT)	1	70	10	20	100
Queensland (QLD)	6	418	60	120	598
South Australia (SA)	3	208	28	59	295
Tasmania (TAS)	2	140	2	20	162
Victoria (VIC)	6	418	58	120	596
Western Australia (WA)	4	280	36	80	396
Total	**30**	**2,092**	**268**	**578**	**2,938**

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 (6)

Alfred Hospital
Austin Health
Gribbles Pathology (Healthscope Pathology)
Monash Medical Centre
Royal Children's 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)
Agar replication
Minimum tests: 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)
Agar replication

4.2.2 SPECIES INCLUDED IN STUDY

Table 3. Species included

Group	Organism	Total
E. coli	*E. coli*	2,092
Klebsiella	*K. pneumoniae*	475
	K. oxytoca	101
	K. pneumoniae subsp *ozaenae*	2
	Total	578
Enterobacter	*E. cloacae*	137
	E. aerogenes	122
	E. asburiae	7
	E. sakazakii	1
	Enterobacter not speciated.	1
	Total	268

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 most recent 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	≤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

Antimicrobial Agent	AST N149 Concentration range	CLSI Breakpoints (mg/L)[a]		
Cefoxitin	≤4, 8, 16, 32, ≥64	≤8	16	≥32
Ceftazidime	≤1, 2, 4, 8, 16, 32, ≥64	≤4	8	≥16
Ertapenem[c]	≤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: Twenty-Second Information Supplement, CLSI document M100-S22, January 2012.

[b] For analysis, breakpoints of ≤4, ≥8 were appied due to the MIC range available on the Vitek card, recognising that the January 2012 breakpoint is actually susceptible ≤ 2 mg/L

[c] 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

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	0.0%	0.8%	1.4%	1.2%	1.4%	2.9%	1.7%	1.1%	1.3%
	%R	51.4%	47.1%	47.1%	36.1%	41.8%	35.7%	46.9%	44.6%	43.4%

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	15.7%	19.7%	15.7%	11.5%	11.5%	11.4%	14.4%	15.7%	14.8%
	%R	7.1%	7.2%	2.9%	4.3%	8.2%	2.1%	8.6%	4.6%	6.2%
***Klebsiella* spp.**	%I	0.0%	3.6%	0.0%	3.3%	5.1%	0.0%	2.5%	0.0%	2.6%
	%R	5.0%	2.9%	0.0%	4.2%	1.7%	0.0%	3.3%	1.3%	2.8%
K. oxytoca	%I	0.0%	0.0%	0.0%	20.0%	0.0%	0.0%	6.9%	0.0%	4.0%
K. oxytoca	%R	0.0%	10.5%	0.0%	0.0%	0.0%	0.0%	10.3%	0.0%	5.0%
K. pneumoniae	%I	0.0%	4.2%	0.0%	1.8%	7.5%	0.0%	1.1%	0.0%	2.3%
K. pneumoniae	%R	5.9%	1.7%	0.0%	4.6%	2.5%	0.0%	1.1%	1.6%	2.3%

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	12.9%	5.1%	4.3%	2.4%	7.2%	0.0%	5.7%	3.2%	4.5%
***Enterobacter* spp.**	%R	0.0%	35.9%	0.0%	16.7%	14.3%	0.0%	20.7%	11.1%	19.8%
E. aerogenes	%R	0.0%	25.0%	0.0%	19.2%	18.2%	-	20.0%	10.0%	17.2%
E. cloacae	%R	0.0%	44.4%	0.0%	16.1%	6.7%	0.0%	22.6%	13.3%	22.6%
***Klebsiella* spp.**	%R	5.0%	1.4%	0.0%	2.5%	3.4%	0.0%	4.2%	1.3%	2.4%
K. oxytoca	%R	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	10.3%	0.0%	3.0%
K. pneumoniae	%R	5.9%	1.7%	0.0%	2.8%	5.0%	0.0%	2.2%	1.6%	2.3%

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	4.3%	3.1%	4.3%	1.9%	4.8%	0.0%	2.4%	3.6%	2.8%
***Enterobacter* spp.**	%R	0.0%	29.7%	0.0%	16.7%	14.3%	0.0%	19.0%	5.6%	17.2%
E. aerogenes	%R	0.0%	32.1%	0.0%	19.2%	18.2%	-	24.0%	0.0%	18.0%
E. cloacae	%R	0.0%	27.8%	0.0%	16.1%	6.7%	0.0%	16.1%	13.3%	16.8%
***Klebsiella* spp.**	%R	0.0%	3.6%	0.0%	5.8%	5.1%	0.0%	5.0%	2.5%	4.0%
K. oxytoca	%R	0.0%	5.3%	0.0%	20.0%	0.0%	0.0%	13.8%	0.0%	6.9%
K. pneumoniae	%R	0.0%	3.3%	0.0%	4.6%	7.5%	0.0%	2.2%	1.6%	3.2%

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	20.0%	18.2%	17.1%	12.2%	16.8%	7.9%	15.6%	15.0%	15.2%
***Enterobacter* spp.**	%R	90.0%	87.5%	80.0%	86.7%	78.6%	50.0%	89.7%	88.9%	86.6%
E. aerogenes	%R	85.7%	78.6%	60.0%	76.9%	72.7%	-	76.0%	90.0%	78.7%
E. cloacae	%R	100%	94.4%	100%	96.8%	80.0%	100%	100%	86.7%	94.2%
***Klebsiella* spp.**	%R	10.0%	16.5%	10.0%	15.0%	23.7%	5.0%	20.0%	21.3%	17.5%
K. oxytoca	%R	33.3%	73.7%	33.3%	80.0%	57.9%	33.3%	69.0%	86.7%	68.3%
K. pneumoniae	%R	5.9%	7.5%	5.9%	9.2%	7.5%	0.0%	4.4%	6.3%	6.7%

Comments:
Interpretation based on MIC range available on Vitek card, which currently do not match those of the CLSI breakpoints published in 2012.
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	2.9%	1.2%	0.0%	2.2%	1.9%	1.4%	2.6%	1.1%	1.8%
***Klebsiella* spp.**	%R	5.0%	2.2%	0.0%	5.0%	1.7%	0.0%	1.7%	2.5%	2.6%
K. oxytoca	%R	0.0%	5.3%	0.0%	10.0%	0.0%	0.0%	0.0%	0.0%	2.0%
K. pneumoniae	%R	5.9%	1.7%	0.0%	4.6%	2.5%	0.0%	2.2%	3.1%	2.7%

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	2.9%	2.9%	2.9%	2.4%	4.3%	0.7%	4.8%	2.9%	3.2%
***Enterobacter* spp.**	%NS	10.0%	42.2%	0.0%	18.3%	14.3%	0.0%	31.0%	13.9%	24.6%
E. aerogenes	%NS	14.3%	32.1%	0.0%	23.1%	18.2%	-	28.0%	10.0%	22.1%
E. cloacae	%NS	0.0%	50.0%	0.0%	16.1%	6.7%	0.0%	35.5%	20.0%	27.7%
***Klebsiella* spp.**	%NS	5.0%	4.3%	5.0%	3.3%	1.7%	0.0%	4.2%	3.8%	3.6%
K. oxytoca	%NS	0.0%	5.3%	0.0%	0.0%	0.0%	0.0%	10.3%	0.0%	4.0%
K. pneumoniae	%NS	5.9%	4.2%	5.9%	3.7%	2.5%	0.0%	2.2%	3.1%	3.4%

Comments: In *E. coli* and *Klebsiella* species non-susceptibility to ceftriaxone is usually 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	1.4%	1.8%	1.4%	1.4%	2.4%	0.7%	2.9%	1.4%	1.9%
***Enterobacter* spp.**	%NS	10.0%	37.5%	0.0%	18.3%	10.7%	0.0%	24.1%	8.3%	20.9%
E. aerogenes	%NS	14.3%	32.1%	0.0%	23.1%	9.1%	-	24.0%	5.0%	19.7%
E. cloacae	%NS	0.0%	41.7%	0.0%	16.1%	6.7%	0.0%	25.8%	13.3%	22.6%
***Klebsiella* spp.**	%NS	5.0%	2.2%	0.0%	2.5%	0.0%	0.0%	0.8%	2.5%	1.7%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%NS	5.9%	2.5%	0.0%	2.8%	0.0%	0.0%	1.1%	1.6%	1.9%

Comments: In *E. coli* and *Klebsiella* species non-susceptibility to ceftazidime is usually 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	1.4%	1.6%	0.0%	0.5%	0.5%	0.0%	0.5%	0.0%	0.7%
***Enterobacter* spp.**	%NS	0.0%	1.6%	0.0%	0.0%	3.6%	0.0%	1.7%	0.0%	1.1%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	-	0.0%	0.0%	0.0%
E. cloacae	%NS	0.0%	2.8%	0.0%	0.0%	0.0%	0.0%	3.2%	0.0%	1.5%
***Klebsiella* spp.**	%NS	0.0%	0.0%	0.0%	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 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%	0.0%	0.0%	0.0%
***Klebsiella* spp.**	%NS	0.0%	0.0%	0.0%	0.8%	0.0%	0.0%	0.0%	0.0%	0.2%
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%	0.0%	0.0%	0.9%	0.0%	0.0%	0.0%	0.0%	0.2%

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

Table 15. Ertapenem

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	0.0%	0.2%	0.0%	0.0%	0.0%	0.0%	0.2%	0.0%	0.1%
***Enterobacter* spp.**	%NS	0.0%	19.4%	0.0%	15.0%	3.6%	0.0%	10.3%	2.8%	10.9%
E. aerogenes	%NS	0.0%	11.1%	0.0%	7.7%	9.1%	-	4.0%	0.0%	5.8%
E. cloacae	%NS	0.0%	25.7%	0.0%	22.6%	0.0%	0.0%	16.1%	6.7%	16.2%
***Klebsiella* spp.**	%NS	5.0%	0.0%	0.0%	0.8%	0.0%	0.0%	0.0%	1.3%	0.5%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%NS	5.9%	0.0%	0.0%	0.9%	0.0%	0.0%	0.0%	1.6%	0.6%

Comments: Non-susceptibility to ertapenem in *Enterobacter* species appeared to have some relationship to stably-derepressed chromosomal AmpC β-lactamase production.

Table 16. Ciprofloxacin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	4.3%	6.1%	5.7%	4.1%	6.7%	2.9%	5.5%	6.1%	5.4%
***Enterobacter* spp.**	%NS	0.0%	3.1%	0.0%	1.7%	7.1%	0.0%	8.6%	5.6%	4.5%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	18.2%	-	0.0%	5.0%	2.5%
E. cloacae	%NS	0.0%	5.6%	0.0%	3.2%	0.0%	0.0%	16.1%	6.7%	6.6%
***Klebsiella* spp.**	%NS	5.0%	1.4%	0.0%	1.7%	0.0%	0.0%	4.2%	3.8%	2.2%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.4%	0.0%	1.0%
K. pneumoniae	%NS	5.9%	1.7%	0.0%	1.8%	0.0%	0.0%	4.4%	3.1%	2.3%

Comments: Ciprofloxacin non-susceptibility indicates 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. Norfloxacin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%NS	4.3%	5.9%	4.3%	3.8%	6.7%	2.9%	5.5%	5.7%	5.2%
***Enterobacter* spp.**	%NS	0.0%	1.6%	0.0%	1.7%	7.1%	0.0%	3.4%	5.6%	3.0%
E. aerogenes	%NS	0.0%	0.0%	0.0%	0.0%	18.2%	-	0.0%	5.0%	2.5%

E. cloacae	%NS	0.0%	2.8%	0.0%	3.2%	0.0%	0.0%	6.5%	6.7%	3.6%
***Klebsiella* spp.**	%NS	5.0%	0.7%	0.0%	1.7%	0.0%	0.0%	4.2%	3.8%	2.1%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.4%	0.0%	1.0%
K. pneumoniae	%NS	5.9%	0.8%	0.0%	1.8%	0.0%	0.0%	4.4%	3.1%	2.1%

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

Table 18. Gentamicin

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	4.3%	4.1%	7.1%	2.9%	6.7%	1.4%	3.8%	5.4%	4.2%
***Enterobacter* spp.**	%R	0.0%	4.7%	0.0%	1.7%	3.6%	0.0%	5.2%	0.0%	3.0%
E. aerogenes	%R	0.0%	3.6%	0.0%	0.0%	0.0%	-	0.0%	0.0%	0.8%
E. cloacae	%R	0.0%	5.6%	0.0%	3.2%	0.0%	0.0%	9.7%	0.0%	4.4%
***Klebsiella* spp.**	%R	5.0%	1.4%	5.0%	0.8%	1.7%	0.0%	1.7%	3.8%	1.9%
K. oxytoca	%R	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
K. pneumoniae	%R	5.9%	1.7%	5.9%	0.9%	2.5%	0.0%	2.2%	4.7%	2.3%

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

Table 19. Trimethoprim

Species		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
E. coli	%R	22.9%	24.4%	14.3%	19.4%	15.9%	16.4%	23.7%	22.1%	21.2%
***Enterobacter* spp.**	%R	10.0%	12.5%	10.0%	8.3%	17.9%	0.0%	19.0%	5.6%	12.3%
E. aerogenes	%R	14.3%	3.6%	0.0%	3.8%	18.2%	-%	16.0%	0.0%	7.4%
E. cloacae	%R	0.0%	19.4%	20.0%	12.9%	6.7%	0.0%	22.6%	13.3%	16.1%
***Klebsiella* spp.**	%R	0.0%	10.1%	15.0%	8.3%	13.6%	10.0%	9.2%	10.0%	9.7%
K. oxytoca	%R	0.0%	5.3%	0.0%	0.0%	15.8%	0.0%	6.9%	0.0%	5.9%
K. pneumoniae	%R	0.0%	10.8%	17.6%	9.2%	12.5%	11.8%	9.9%	12.5%	10.5%

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).

E. coli

Ampicillin resistance proportions have been moderately high for more than a decade, and approximately stable at around 44% in the Australian community. Amoxycillin-clavulanate intermediate and resistant strains have been around for some time but remain in relatively low proportion. Percentages of resistance to ticarcillin-clavulanate and piperacillin-tazobactam remain low for *E. coli*. Modest levels of resistance are present to cefazolin. Ciprofloxacin resistance is increasing despite controlled usage in both the community and in hospitals, although there is increasing use of this antimicrobial as a topical agent. Gentamicin resistance remains relatively low despite more three decades of use in mostly hospital practice. Trimethoprim, especially as cotrimoxazole, use has been high in the community and this is reflected in the resistance percentages.

***Klebsiella* species**

Percentages of resistance to ticarcillin-clavulanate and piperacillin-tazobactam remain low for *Klebsiella* spp. Acquired resistances of interest include those of ß-lactamase inhibitor combinations; percentage of resistance to amoxycillin-clavulanate and piperacillin-tazobactam are still low. Percentages are substantially higher for cefazolin, a first generation cephalosporin. Resistance to gentamicin remains low.

***Enterobacter* species**

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

6.3 MAJOR RESISTANCES

6.3.1 ESBLS

Extended-spectrum ß-lactamases are important problem resistances internationally. Previously, they were 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 ESBLs 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 increasing 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 of ceftriaxone nor ceftazidime testing will identify ESBL production in *Enterobacter* species because of their chromosomal AmpC β-lactamases. In that species, cefepime at 1 mg/L is suggestive that an isolate of this genus habours 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 that encode ESBLs. Similarly, SHV screening does not discriminate between SHV-1, -11, which are narrow-spectrum β-lactamases, and SHV genes that encode ESBLs. SHV-1 is the natural chromosomal enzyme of *K. pneumoniae* enzyme leading to natural ampicillin/amoxycillin resistance. 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	14	2	12	9	1	23	9	72
Ceftriaxone > 1 mg/L	2.9%	2.9%	2.9%	2.4%	4.3%	0.7%	4.8%	2.9%	3.2%
Ceftazidime > 1 mg/L	2.9%	2.5%	1.4%	2.4%	2.9%	0.7%	4.3%	2.9%	2.8%
Either of above	2.9%	2.9%	2.9%	2.9%	4.3%	0.7%	5.5%	3.2%	3.4%
Confirmed									
any ESBL (No. received)	2/2	14/14	2/2	9/10	9/9	1/1	18/20	9/9	65/69
CTX-M types	2	13	2	7	6	1	13	7	51
plasmid-borne AmpC	0	1	0	2	2	0	3	0	8
SHV	0	0	0	0	0	0	1	0	1
Klebsiella pneumoniae	1	6	1	4	1	0	2	2	17
Ceftriaxone > 1 mg/L	5.9%	4.2%	5.9%	3.7%	2.5%		2.2%	3.1%	3.4%
Ceftazidime > 1 mg/L	5.9%	4.2%	0.0%	2.8%	0.0%		1.1%	1.6%	2.3%
Either of above	5.9%	5.0%	5.9%	3.7%	2.5%		2.2%	3.1%	3.6%
Confirmed									
any ESBL (No. received)	1/1	6/6	1/1	4/4	1/1		2/2	2/2	17/17
CTX-M types	0	5	1	2	1		1	2	12
plasmid-borne AmpC	0	1	0	1	0		0	0	2
TEM	1	3	0	1	0		2	0	7
Klebsiella oxytoca	0	1	0	0	0	0	3	0	4
Ceftriaxone > 1 mg/L		5.3%					10.3%		4.0%
Ceftazidime > 1 mg/L		0.0%					3.4%		1.0%
Either of above		5.3%					10.3%		4.0%
Confirmed									
any ESBL (No. received)		0/1					0/2		0/3
CTX-M types		0					0		0
plasmid-borne AmpC		0					0		0
***Enterobacter* species**	1	6	0	0	2	0	2	1	12
Cefepime > 1 mg/L	10.0%	9.4%			7.1%		3.4%	2.8%	4.5%
Confirmed									
any ESBL (No. received)	1/1	2/6			0/2		2/2	0	5/12
CTX-M types	1	1			0		2	0	4
SHV	0	1			0		0	0	1
TEM	1	1			0		2	0	4

* Strains may possess more than one type of ESBL gene

Based on the tests performed in this study, ESBLs were found equally among *Klebsiella* species (3.0% confirmed) and *E. coli* (3.1% confirmed). For the *Enterobacter* species 2.4% of isolates contained an ESBL. There was a notable presence of CTX-M enzymes in *E. coli* (51/65 tested).

All of the *K. oxytoca* isolates with an ESBL phenotype were hyperproducers of K1 β-lactamase, the natural chromosomal enzyme in these 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 β-lactamase Production

Species	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Australia
Escherichia coli	2	6	0	9	4	2	11	3	37
Cefoxitin ≥ 32 mg/L	2.9%	1.2%	0.0%	2.2%	1.9%	1.4%	2.6%	1.1%	1.8%
***Klebsiella* species**	1	3	0	6	1	0	2	2	15
Cefoxitin ≥ 32 mg/L	5.0%	2.2%	0.0%	5.0%	1.7%	0.0%	1.7%	2.5%	2.6%

The proportions of *E. coli* and *Klebsiella* species with elevated cefoxitin MICs were low. Only 24% of cefoxitin-resistant *E. coli* and 13% of *Klebsiella* spp. that were available for molecular confirmation were confirmed to contain plasmid-borne AmpC; with CIT (n=9) in *E. coli,* and one CIT plus DHA detected 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. Two *K. pneumoniae* and one *E. cloacae* in the survey contained $bla_{\text{IMP-4}}$ (MIC range 0.5 to 2 mg/L). Only one isolate (*K. pneumoniae*) was non-susceptible to meropenem. No VIM, KPC, OXA-48-like or NDM genes were 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=63)	%I	1.6%	3.2%	-
	%R	60.3%	49.2%	68.3%
Klebsiella pneumoniae (n=20)	%I	5.0%	0.0%	-
	%R	25.0%	45.0%	65.0%

* 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. Multi-resistance in *E. coli* increased from 4.5% in 2008 to 7.2% in this study.

Table 23. Mutli-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	30	19	9	7	92.9%	2	2					1					7.1%
NSW	488	228	90	103	33	93.0%	19	1	6	1	6		1					7.0%
NT	70	35	14	14	3	94.3%	1	2		1								5.7%
QLD	418	242	80	56	12	93.3%	13	8	4	3								6.7%
SA	208	115	38	21	10	88.5%	10	6	7		1							11.5%
TAS	140	83	30	20	4	97.9%	2			1								2.1%
VIC	418	197	84	86	19	92.3%	9	8	8	4	1	2						7.7%
WA	280	143	52	48	17	92.9%	10	5	1	3		1						7.1%
Total	*2092*	*1073*	*407*	*357*	*105*	*92.8%*	*66*	*32*	*26*	*13*	*8*	*3*	*2*					*7.2%*

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.. Mutli-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	9	10			95.0%				1							5.0%
NSW	139	68	55	6	3	95.0%	5	1		1							5.0%
NT	20	10	6	3	1	100%											0.0%
QLD	120	67	33	13	2	95.8%	2	1	1			1					4.2%
SA	59	32	18	5	1	94.9%	3										5.1%
TAS	20	11	8	1		100%											
VIC	120	56	48	6	5	95.8%	2	1	1	1							4.2%
WA	80	39	31	3	3	95.0%	1	3									5.0%
Total	*578*	*292*	*209*	*37*	*15*	*95.7%*	*13*	*6*	*2*	*3*		*1*					*4.3%*

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. Mutli-resistance in Enterobacter species

		Non-multi-resistant					Multi-resistant							
Region	***Total***	***0***	***1***	***2***	***3***	***%***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***%***
ACT	10	6	3		1	100%								
NSW	64	14	24	8	9	85.9%	7	2						14.1%
NT	10	2	8			100%								
QLD	60	30	18	1	6	91.7%	4	1						8.3%
SA	28	13	9	3	1	92.9%		2						7.1%
TAS	2	2				100%								
VIC	58	21	18	6	6	87.9%	3	2	2					12.1%
WA	36	20	12	2	2	100%								
Total	*268*	*108*	*92*	*20*	*25*	*91.4%*	*14*	*7*	*2*					*8.6%*

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. Nevertheless, isolates were included only if there was laboratory evidence of urinary tract infection, although some cases of asymptomatic bacteriuria were likely included.

7 STANDARDS AND INFORMATION RESOURCES

1. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twenty-Second 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 STATE

Ampicillin

Genus	State	Total	%S	%I	%R
Enterobacter species	ACT	10	30.0%	60.0%	10.0%
	NSW	64	18.8%	18.8%	62.5%
	NT	10	20.0%	40.0%	40.0%
	QLD	60	21.7%	31.7%	46.7%
	SA	28	42.9%	14.3%	42.9%
	TAS	2	50.0%	0.0%	50.0%
	VIC	58	27.6%	22.4%	50.0%
	WA	36	22.2%	25.0%	52.8%
	National	268	67	67	134
			25.0%	25.0%	50.0%
Escherichia coli	ACT	70	48.6%	0.0%	51.4%
	NSW	488	52.0%	0.8%	47.1%
	NT	70	51.4%	1.4%	47.1%
	QLD	418	62.7%	1.2%	36.1%
	SA	208	56.7%	1.4%	41.8%
	TAS	140	61.4%	2.9%	35.7%
	VIC	418	51.4%	1.7%	46.9%
	WA	280	54.3%	1.1%	44.6%
	National	2092	1157	27	908
			55.3%	1.3%	43.4%
Klebsiella species	ACT	20	0.0%	40.0%	60.0%
	NSW	139	3.6%	30.2%	66.2%
	NT	20	0.0%	35.0%	65.0%
	QLD	120	3.3%	34.2%	62.5%
	SA	59	5.1%	39.0%	55.9%
	TAS	20	10.0%	25.0%	65.0%
	VIC	120	6.7%	31.7%	61.7%
	WA	80	3.8%	31.3%	65.0%
	National	578	25	189	364
			4.3%	32.7%	63.0%

Amoxycillin-clavulanate

Genus	State	Total	%S	%I	%R
Enterobacter species	ACT	10	10.0%	10.0%	80.0%
	NSW	64	12.5%	7.8%	79.7%
	NT	10	10.0%	10.0%	80.0%
	QLD	60	10.0%	3.3%	86.7%
	SA	28	25.0%	14.3%	60.7%
	TAS	2	50.0%	0.0%	50.0%
	VIC	58	13.8%	5.2%	81.0%
	WA	36	11.1%	8.3%	80.6%
	National	268	36	19	213
			13.4%	7.1%	79.5%
Escherichia coli	ACT	70	77.1%	15.7%	7.1%
	NSW	488	73.2%	19.7%	7.2%
	NT	70	81.4%	15.7%	2.9%
	QLD	418	84.2%	11.5%	4.3%
	SA	208	80.3%	11.5%	8.2%
	TAS	140	86.4%	11.4%	2.1%
	VIC	418	77.0%	14.4%	8.6%
	WA	280	79.6%	15.7%	4.6%
	National	2092	1653	310	129
			79.0%	14.8%	6.2%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	93.5%	3.6%	2.9%
	NT	20	100%		
	QLD	120	92.5%	3.3%	4.2%
	SA	59	93.2%	5.1%	1.7%
	TAS	20	100%		
	VIC	120	94.2%	2.5%	3.3%
	WA	80	98.8%	0.0%	1.3%
	National	578	547	15	16
			94.6%	2.6%	2.8%

Ticarcillin-clavulanate

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	64	56.3%	7.8%	35.9%
	NT	10	80.0%	20.0%	0.0%
	QLD	60	80.0%	3.3%	16.7%
	SA	28	85.7%	0.0%	14.3%
	TAS	2	100%		
	VIC	58	69.0%	10.3%	20.7%
	WA	36	80.6%	8.3%	11.1%
	National	268	197	18	53
			73.5%	6.7%	19.8%
Escherichia coli	ACT	70	81.4%	5.7%	12.9%
	NSW	488	84.0%	10.9%	5.1%
	NT	70	91.4%	4.3%	4.3%
	QLD	418	90.2%	7.4%	2.4%
	SA	208	88.0%	4.8%	7.2%
	TAS	140	96.4%	3.6%	0.0%
	VIC	418	87.8%	6.5%	5.7%
	WA	280	90.4%	6.4%	3.2%
	National	2092	1846	151	95
			88.2%	7.2%	4.5%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	95.0%	3.6%	1.4%
	NT	20	100%		
	QLD	120	94.2%	3.3%	2.5%
	SA	59	93.2%	3.4%	3.4%
	TAS	20	100%		
	VIC	120	95.0%	0.8%	4.2%
	WA	80	97.5%	1.3%	1.3%
	National	578	551	13	14
			95.3%	2.2%	2.4%

Piperacillin-tazobactam

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	64	65.6%	4.7%	29.7%
	NT	10	100%		
	QLD	60	81.7%	1.7%	16.7%
	SA	28	85.7%	0.0%	14.3%
	TAS	2	100%		
	VIC	58	79.3%	1.7%	19.0%
	WA	36	91.7%	2.8%	5.6%
	National	268	216	6	46
			80.6%	2.2%	17.2%
Escherichia coli	ACT	70	94.3%	1.4%	4.3%
	NSW	488	96.5%	0.4%	3.1%
	NT	70	95.7%	0.0%	4.3%
	QLD	418	98.1%	0.0%	1.9%
	SA	208	94.7%	0.5%	4.8%
	TAS	140	100%		
	VIC	418	96.4%	1.2%	2.4%
	WA	280	96.1%	0.4%	3.6%
	National	2092	2023	10	59
			96.7%	0.5%	2.8%
Klebsiella species	ACT	20	95.0%	5.0%	0.0%
	NSW	139	96.4%	0.0%	3.6%
	NT	20	100%		
	QLD	120	92.5%	1.7%	5.8%
	SA	59	94.9%	0.0%	5.1%
	TAS	20	100%		
	VIC	120	95.0%	0.0%	5.0%
	WA	80	97.5%	0.0%	2.5%
	National	578	552	3	23
			95.5%	0.5%	4.0%

Cefazolin

Genus	Region	Total	%S+I	%R
Enterobacter species	ACT	10	10.0%	90.0%
	NSW	64	12.5%	87.5%
	NT	10	20.0%	80.0%
	QLD	60	13.3%	86.7%
	SA	28	21.4%	78.6%
	TAS	2	50.0%	50.0%
	VIC	58	10.3%	89.7%
	WA	36	11.1%	88.9%
	National	268	36	232
			13.4%	86.6%
Escherichia coli	ACT	70	80.0%	20.0%
	NSW	488	81.8%	18.2%
	NT	70	82.9%	17.1%
	QLD	418	87.6%	12.2%
	SA	208	83.2%	16.8%
	TAS	140	92.1%	7.9%
	VIC	418	84.4%	15.6%
	WA	280	85.0%	15.0%
	National	2092	1773	319
			84.8%	15.2%
Klebsiella species	ACT	20	90.0%	10.0%
	NSW	139	83.5%	16.5%
	NT	20	90.0%	10.0%
	QLD	120	85.0%	15.0%
	SA	59	76.3%	23.7%
	TAS	20	95.0%	5.0%
	VIC	120	80.0%	20.0%
	WA	80	78.8%	21.3%
	National	578	477	101
			82.5%	17.5%

Cefoxitin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	0.0%	0.0%	100%
	NSW	64	7.8%	1.6%	90.6%
	NT	10	10.0%	0.0%	90.0%
	QLD	60	6.7%	0.0%	93.3%
	SA	28	25.0%	3.6%	71.4%
	TAS	2	50.0%	0.0%	50.0%
	VIC	58	6.9%	1.7%	91.4%
	WA	36	8.3%	0.0%	91.7%
	National	268	25	3	240
			9.3%	1.1%	89.6%
Escherichia coli	ACT	70	95.7%	1.4%	2.9%
	NSW	488	95.5%	3.3%	1.2%
	NT	70	94.3%	5.7%	0.0%
	QLD	418	95.7%	2.2%	2.2%
	SA	208	96.6%	1.4%	1.9%
	TAS	140	98.6%	0.0	1.4%
	VIC	418	95.2%	2.2%	2.6%
	WA	280	96.4%	2.5%	1.1%
	National	2092	2006	49	37
			95.9%	2.3%	1.8%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	97.1%	0.7%	2.2%
	NT	20	100%		
	QLD	120	93.3%	1.7%	5.0%
	SA	59	94.9%	3.4%	1.7%
	TAS	20	100%		
	VIC	120	95.0%	3.3%	1.7%
	WA	80	96.3%	1.3%	2.5%
	National	578	553	10	15
			95.7%	1.7%	2.6%

Ceftriaxone

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	90.0%	0.0%	10.0%
	NSW	64	57.8%	1.6%	40.6%
	NT	10	100%		
	QLD	60	81.7%	0.0%	18.3%
	SA	28	85.7%	0.0%	14.3%
	TAS	2	100%		
	VIC	58	69.0%	1.7%	29.3%
	WA	36	86.1%	0.0%	13.9%
	National	268	202	2	64
			75.4%	0.7%	23.9%
Escherichia coli	ACT	70	97.1%	0.0%	2.9%
	NSW	488	97.1%	0.0%	2.9%
	NT	70	97.1%	0.0%	2.9%
	QLD	418	97.6%	0.0%	2.4%
	SA	208	95.7%	0.0%	4.3%
	TAS	140	99.3%	0.0%	0.7%
	VIC	418	95.2%	0.0%	4.8%
	WA	280	97.1%	0.0%	2.9%
	National	2092	2026	0	66
			96.8%	0.0%	3.2%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	95.7%	0.0%	4.3%
	NT	20	95.0%	0.0%	5.0%
	QLD	120	96.7%	0.0%	3.3%
	SA	59	98.3%	0.0%	1.7%
	TAS	20	100%		
	VIC	120	95.8%	0.8%	3.3%
	WA	80	96.3%	0.0%	3.8%
	National	578	557	1	20
			96.4%	0.2%	3.5%

Ceftazidime

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	90.0%	0.0%	10.0%
	NSW	64	62.5%	6.3%	31.3%
	NT	10	100%		
	QLD	60	81.7%	1.7%	16.7%
	SA	28	89.3%	0.0%	10.7%
	TAS	2	100%		
	VIC	58	75.9%	5.2%	19.0%
	WA	36	91.7%	0.0%	8.3%
	National	268	212	8	48
			79.1%	3.0%	17.9%
Escherichia coli	ACT	70	98.6%	0.0%	1.4%
	NSW	488	98.2%	0.2%	1.6%
	NT	70	98.6%	0.0%	1.4%
	QLD	418	98.6%	0.2%	1.2%
	SA	208	97.6%	0.0%	2.4%
	TAS	140	99.3%	0.0%	0.7%
	VIC	418	97.1%	0.0%	2.9%
	WA	280	98.6%	0.0%	1.4%
	National	2092	2053	2	37
			98.1%	0.1%	1.8%
Klebsiella species	ACT	20	95.0%		5.0%
	NSW	139	97.8%		2.2%
	NT	20	100%		
	QLD	120	97.5%		2.5%
	SA	59	100%		
	TAS	20	100%		
	VIC	120	99.2%		0.8%
	WA	80	97.5%		2.5%
	National	578	568	0	10
			98.3%	0.0%	1.7%

Cefepime

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	64	98.4%	1.6%	0.0%
	NT	10	100%		
	QLD	60	100%		
	SA	28	96.4%	0.0%	3.6%
	TAS	2	100%		
	VIC	58	98.3%	0.0%	1.7%
	WA	36	100%		
	National	268	265	1	2
			98.9%	0.4%	0.7%
Escherichia coli	ACT	70	98.6%	0.0%	1.4%
	NSW	488	98.4%	0.0%	1.6%
	NT	70	100%		
	QLD	418	99.5%	0.0%	0.5%
	SA	208	99.5%	0.0%	0.5%
	TAS	140	100%		
	VIC	418	99.5%	0.0%	0.5%
	WA	280	100%		
	National	2092	2078	0	14
			99.3%	0.0%	0.7%
Klebsiella species	ACT	20	100%		
	NSW	139	100%		
	NT	20	100%		
	QLD	120	100%		
	SA	59	100%		
	TAS	20	100%		
	VIC	120	100%		
	WA	80	100%		
	National	578	578		
			100%		

Meropenem

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	64	100%		
	NT	10	100%		
	QLD	60	100%		
	SA	28	100%		
	TAS	2	100%		
	VIC	58	100%		
	WA	36	100%		
	National	268	268		
			100%		
Escherichia coli	ACT	70	100%		
	NSW	488	100%		
	NT	70	100%		
	QLD	418	100%		
	SA	208	100%		
	TAS	140	100%		
	VIC	418	100%		
	WA	280	100%		
	National	2092	2092		
			100%		
Klebsiella species	ACT	20	100%		
	NSW	139	100%		
	NT	20	100%		
	QLD	120	99.2%	0.8%	0.0%
	SA	59	100%		
	TAS	20	100%		
	VIC	120	100%		
	WA	80	100%		
	National	578	577	1	0
			99.8%	0.2%	0.0%

Ciprofloxacin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	64	96.9%	1.6%	1.6%
	NT	10	100%		
	QLD	60	98.3%	0.0%	1.7%
	SA	28	92.9%	3.6%	3.6%
	TAS	2	100%		
	VIC	58	91.4%	5.2%	3.4%
	WA	36	94.4%	2.8%	2.8%
	National	268	256	6	6
			95.5%	2.2%	2.2%
Escherichia coli	ACT	70	95.7%	0.0%	4.3%
	NSW	488	93.9%	0.2%	5.9%
	NT	70	94.3%	1.4%	4.3%
	QLD	418	95.9%	0.2%	3.8%
	SA	208	93.3%	0.0%	6.7%
	TAS	140	97.1%	0.0%	2.9%
	VIC	418	94.5%	0.2%	5.3%
	WA	280	93.9%	0.0%	6.1%
	National	2092	1980	4	108
			94.6%	0.2%	5.2%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	98.6%	0.7%	0.7%
	NT	20	100%		
	QLD	120	98.3%	0.0%	1.7%
	SA	59	100%		
	TAS	20	100%		
	VIC	120	95.8%	0.0%	4.2%
	WA	80	96.3%	0.0%	3.8%
	National	578	565	1	12
			97.8%	0.2%	2.1%

Norfloxacin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	64	98.4%	1.6%	0.0%
	NT	10	100%		
	QLD	60	98.3%	0.0%	1.7%
	SA	28	92.9%	7.1%	0.0%
	TAS	2	100%		
	VIC	58	96.6%	1.7%	1.7%
	WA	36	94.4%	2.8%	2.8%
	National	268	260	5	3
			97.0%	1.9%	1.1%
Escherichia coli	ACT	70	95.7%	0.0%	4.3%
	NSW	488	94.1%	0.2%	5.7%
	NT	70	95.7%	0.0%	4.3%
	QLD	418	96.2%	0.2%	3.6%
	SA	208	93.3%	0.5%	6.3%
	TAS	140	97.1%	0.0%	2.9%
	VIC	418	94.5%	0.7%	4.8%
	WA	280	94.3%	0.0%	5.7%
	National	2092	1984	6	102
			94.8%	0.3%	4.9%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	99.3%	0.0%	0.7%
	NT	20	100%		
	QLD	120	98.3%	0.0%	1.7%
	SA	59	100%		
	TAS	20	100%		
	VIC	120	95.8%	1.7%	2.5%
	WA	80	96.3%	1.3%	2.5%
	National	578	566	3	9
			97.9%	0.5%	1.6%

Gentamicin

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	64	95.3%	0.0%	4.7%
	NT	10	100%		
	QLD	60	98.3%	0.0%	1.7%
	SA	28	96.4%	0.0%	3.6%
	TAS	2	100%		
	VIC	58	94.8%	0.0%	5.2%
	WA	36	100%		
	National	268	260	0	8
			97.0%	0.0%	3.0%
Escherichia coli	ACT	70	95.7%	0.0%	4.3%
	NSW	488	95.3%	0.6%	4.1%
	NT	70	92.9%	0.0%	7.1%
	QLD	418	97.1%	0.0%	2.9%
	SA	208	93.3%	0.0%	6.7%
	TAS	140	97.9%	0.7%	1.4%
	VIC	418	95.9%	0.2%	3.8%
	WA	280	94.6%	0.0%	5.4%
	National	2092	2000	5	87
			95.6%	0.2%	4.2%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	98.6%	0.0%	1.4%
	NT	20	95.0%	0.0%	5.0%
	QLD	120	99.2%	0.0%	0.8%
	SA	59	98.3%	0.0%	1.7%
	TAS	20	100%		
	VIC	120	98.3%	0.0%	1.7%
	WA	80	96.3%	0.0%	3.8%
	National	578	567	0	11
			98.1%	0.0%	1.9%

Trimethoprim

Genus	Region	Total	%S	%R
Enterobacter species	ACT	10	90.0%	10.0%
	NSW	64	87.5%	12.5%
	NT	10	90.0%	10.0%
	QLD	60	91.7%	8.3%
	SA	28	82.1%	17.9%
	TAS	2	100%	
	VIC	58	81.0%	19.0%
	WA	36	94.4%	5.6%
	National	268	235	33
			87.7%	12.3%
Escherichia coli	ACT	70	77.1%	22.9%
	NSW	488	75.6%	24.4%
	NT	70	85.7%	14.3%
	QLD	418	80.6%	19.4%
	SA	208	84.1%	15.9%
	TAS	140	83.6%	16.4%
	VIC	418	76.3%	23.7%
	WA	280	77.9%	22.1%
	National	2092	1649	443
			78.8%	21.2%
Klebsiella species	ACT	20	100%	
	NSW	139	89.9%	10.1%
	NT	20	85.0%	15.0%
	QLD	120	91.7%	8.3%
	SA	59	86.4%	13.6%
	TAS	20	90.0%	10.0%
	VIC	120	90.8%	9.2%
	WA	80	90.0%	10.0%
	National	578	522	56
			90.3%	9.7%

Ertapenem

Genus	Region	Total	%S	%I	%R
Enterobacter species	ACT	10	100%		
	NSW	62	80.6%	12.9%	6.5%
	NT	9	100%		
	QLD	60	85.0%	8.3%	6.7%
	SA	28	96.4%	0.0%	3.6%
	TAS	2	100%		
	VIC	58	89.7%	6.9%	3.4%
	WA	36	97.2%	2.8%	0.0%
	National	265	236	18	11
			89.1%	6.8%	4.2%
Escherichia coli	ACT	70	100%		
	NSW	488	99.8%	0.2%	0.0%
	NT	70	100%		
	QLD	418	100%		
	SA	207	100%		
	TAS	140	100%		
	VIC	418	99.8%	0.2%	0.0%
	WA	280	100%		
	National	2091	2089	2	0
			99.9%	0.1%	0.0%
Klebsiella species	ACT	20	95.0%	0.0%	5.0%
	NSW	139	100%		
	NT	20	100%		
	QLD	120	99.2%	0.0%	0.8%
	SA	59	100%		
	TAS	20	100%		
	VIC	117	100%		
	WA	80	98.8%	1.3%	0.0%
	National	575	572	1	2
			99.5%	0.2%	0.3%

APPENDIX 2. ANTIBIOTIC PROFILES BY FREQUENCY

***Enterobacter* species** (n = 268)

Antibiotic Profile	State								
PtzCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
Nit	152	39	25	8	32	1	15	23	9
PtzCtrCaz Nit	31	6	16		6		1	2	
	28	7	5	1	4	1	5	5	
TmpNit	10	2	5		2				1
Ctr Nit	6		3		1			2	
PtzCtrCaz	5	2	2					1	
PtzCtrCaz TmpNit	5	3			1		1		
Tmp	3				1		1	1	
Cip	2		1					1	
CtrCaz	2		1		1				
CtrCaz Nit	2		1		1				
PtzCtrCaz Gen TmpNitCip	2		1		1				
NitCip	1						1		
Tmp Cip	1							1	
TmpNitCip	1						1		
Gen NitCip	1	1							
Gen Tmp	1						1		
Ctr	1				1				
Ctr Tmp Cip	1				1				
Ctr TmpNit	1				1				
Ctr TmpNitCip	1				1				
CtrCaz TmpNit	1			1					
CtrCaz Gen TmpNit	1		1						
Ptz TmpNit	1		1						
Ptz Caz Nit	1				1				
PtzCtr	1						1		
PtzCtrCaz TmpNitCip	1				1				
PtzCtrCaz Gen Nit	1		1						
PtzCtrCaz Gen TmpNit	1				1				
PtzCtrCazCpm Nit	1		1						
PtzCtrCazCpm TmpNit	1						1		
PtzCtrCazCpmGen TmpNitCip	1				1				

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

Escherichia coli (n = 2,092)

				1025	228	220	29	188	77	113	136	34
Amp				242	45	39	13	49	21	31	33	11
Amp			Tmp	142	20	42	3	33	8	8	25	3
AmpAmc	Czl			116	16	39	4	25	6	11	11	4
AmpAmc				98	15	30	2	28	5	4	13	1
			Tmp	75	18	18	4	17	5	5	7	1
AmpAmc	Czl		Tmp	29	4	13	3	2	1	1	4	1
AmpAmc			Tmp	26	3	10		5	2	4	1	1
			Nit	20	6	3	1	4	2		3	1
AmpAmcPtzCzl				20		7	2	1		6	3	1
AmpAmc	CzlCfx			19	3	6	1	2	2	1	3	1
Amp	Czl			13	5	4	1	1				2
AmpAmcPtzCzl			Tmp	13	5	1	1	4			2	
Amp			Nit	11	2	1		4	2		2	
Amp			Tmp Cip	11	2	3		1	2	2	1	
Amp		Gen	Tmp	11		4		3		2	2	
Amp			TmpNit	10	3	1	1	5				
	Cfx			9	5	1		2			1	
Amp		Gen	Tmp Cip	9	3	1		2		1	2	
Amp	Czl		Tmp	7	1			3	1		2	
AmpAmc		Gen	Tmp	7	2	1	1	1	1		1	
			Cip	6	1	4					1	
Amp			Cip	6	1	3		1			1	
AmpAmcPtz			Tmp	6	3	3						
			Tmp Cip	5	1	1		2	1			
AmpAmc			TmpNit	5	1	1		2			1	
AmpAmc	CzlCfxCtrCaz			5	1	1		3				
			TmpNit	4	1			1	1		1	
Amp		Gen		4					1	1	1	1
AmpAmc	Czl Ctr	Gen	Tmp	4	1	1		1				1
AmpAmc	CzlCfx		Tmp	4	1	1		1			1	
Amc				3		2					1	
Amp	Cfx			3	2	1						
Amp	Czl	Gen	Tmp	3	1					1	1	
AmpAmc			Nit	3	1	1			1			
AmpAmc	Czl		Cip	3				1			2	
AmpAmc	Czl		TmpNit	3				2			1	
AmpAmc	Czl CtrCaz	Gen	Cip	3						3		
AmpAmcPtzCzlCfxCtrCaz			Tmp Cip	3				1		1	1	
		Gen	Tmp	2		1					1	
Amp		Gen	TmpNitCip	2				1				1
Amp	Cfx		Tmp Cip	2		1						1
Amp	Cfx	Gen	Tmp Cip	2		1				1		
Amp	Czl Ctr		Tmp Cip	2	1						1	
Amp	Czl Ctr	Gen	Tmp Cip	2	1			1				
Amp	Czl CtrCaz	Gen	Tmp	2				1		1		
AmpAmc		Gen		2							1	1

Antibiotic Profile		State							
AmpAmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
AmpAmc Gen Tmp Cip	2				1			1	
AmpAmc Cfx	2	1			1				
AmpAmc Czl Gen Tmp	2	1					1		
AmpAmc Czl Gen Tmp Cip	2						2		
AmpAmc Czl Ctr Gen Tmp Cip	2		1					1	
AmpAmc Czl CtrCaz Gen Tmp Cip	2	1				1			
AmpAmc Czl CtrCazCpmGen Tmp	2	1	1						
AmpAmc CzlCfx TmpNitCip	2	1					1		
AmpAmc CzlCfxCtr TmpNit	2		1		1				
AmpAmcPtzCzl Ctr Gen Tmp Cip	2				2				
AmpAmcPtzCzlCfx	2				1				1
AmpAmcPtzCzlCfxCtrCazCpmGen TmpNitCip	2			1	1				
TmpNitCip	1		1						
Gen	1		1						
Gen Tmp Cip	1		1						
Cfx Tmp	1		1						
Czl	1	1							
Czl Cip	1				1				
CzlCfx	1	1							
Amc CzlCfx Nit	1							1	
Amp NitCip	1								1
Amp Gen Cip	1		1						
Amp Gen TmpNit	1			1					
Amp Cfx GenAmk Cip	1		1						
Amp CfxCtrCaz	1	1							
Amp Czl Cip	1						1		
Amp Czl Caz TmpNit	1				1				
Amp Czl Ctr	1				1				
Amp Czl Ctr Gen Tmp	1							1	
Amp Czl CtrCaz	1							1	
Amp Czl CtrCaz Tmp Cip	1	1							
Amp Czl CtrCazCpm Tmp Cip	1	1							
Amp CzlCfxCtr Tmp Cip	1			1					
Amp CzlCfxCtrCaz Gen Tmp Cip	1		1						
Amp Ptz	1								1
Amp PtzCzl Tmp	1		1						
AmpAmc Cip	1			1					
AmpAmc Tmp Cip	1	1							
AmpAmc Gen Cip	1				1				
AmpAmc Gen TmpNitCip	1	1							
AmpAmc Cfx Cip	1							1	
AmpAmc Czl Nit	1	1							
AmpAmc Czl Tmp Cip	1							1	
AmpAmc Czl Ctr Tmp Cip	1						1		
AmpAmc Czl Ctr Cpm Tmp Cip	1		1						
AmpAmc Czl CtrCaz Gen TmpNitCip	1							1	
AmpAmc Czl CtrCazCpmGen Cip	1		1						

Antibiotic Profile	State								
AmpAmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
AmpAmc CzlCfx Nit	1		1						
AmpAmc CzlCfx Tmp Cip	1	1							
AmpAmc CzlCfx Gen Tmp Cip	1		1						
AmpAmc CzlCfx Gen TmpNitCip	1						1		
AmpAmc CzlCfxCtr	1	1							
AmpAmc CzlCfxCtr Cip	1				1				
AmpAmc CzlCfxCtr Gen Cip	1				1				
AmpAmc CzlCfxCtr CpmGen TmpNitCip	1		1						
AmpAmc CzlCfxCtrCaz Cip	1				1				
AmpAmc CzlCfxCtrCaz Gen TmpNitCip	1								1
AmpAmc CzlCfxCtrCazCpm Cip	1				1				
AmpAmc CzlCfxCtrCazCpmGen TmpNitCip	1		1						
AmpAmcPtz	1							1	
AmpAmcPtz Nit	1						1		
AmpAmcPtz Cfx Tmp Cip	1				1				
AmpAmcPtzCzl Nit	1							1	
AmpAmcPtzCzl Ctr	1						1		
AmpAmcPtzCzl Ctr Tmp Cip	1				1				
AmpAmcPtzCzl Ctr Gen TmpNitCip	1							1	
AmpAmcPtzCzl CtrCaz TmpNitCip	1		1						
AmpAmcPtzCzl CtrCaz Gen Tmp Cip	1				1				
AmpAmcPtzCzl CtrCazCpm Cip	1		1						
AmpAmcPtzCzl CtrCazCpmGen Cip	1		1						
AmpAmcPtzCzlCfx NitCip	1							1	
AmpAmcPtzCzlCfx Gen Tmp Cip	1		1						
AmpAmcPtzCzlCfxCtr	1						1		
AmpAmcPtzCzlCfxCtr Cpm	1						1		
AmpAmcPtzCzlCfxCtrCaz	1				1				
AmpAmcPtzCzlCfxCtrCaz Tmp	1				1				
AmpAmcPtzCzlCfxCtrCaz Gen TmpNitCip	1							1	
AmpAmcPtzCzlCfxCtrCazCpmGen Tmp Cip	1		1						

Amp = ampicillin, Amc = amoxycillin-clavulanate, 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

***Klebsiella* species** (n = 578)

Antibiotic Profile	State								
AmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD	NSW	ACT	VIC	TAS	SA	WA	NT
Nit	332	72	82	16	65	13	26	44	14
	92	18	23	2	20	4	14	10	1
Czl	31	5	7		4	1	3	10	1
TmpNit	28	4	8		5	2	2	4	3
Czl Nit	25	2	4	1	10		5	3	
Cfx Nit	8	3	1		2			2	
AmcPtzCzl Nit	6	2	2		2				
Czl Ctr Gen TmpNit	4		1		1		1	1	
CzlCfx Nit	4	1	1				1	1	
Tmp	3	2					1		
Czl TmpNit	2		1		1				
Ptz Nit	2	2							
Amc Nit	2		1				1		
Amc CzlCfx Nit	2	1	1						
AmcPtz TmpNit	2	1					1		
AmcPtzCzl	2	2							
AmcPtzCzl Ctr	2		1		1				
NitCip	1				1				
TmpNitCip	1							1	
GenAmkTmpNitCip	1							1	
Cfx NitCip	1				1				
Cfx TmpNit	1				1				
Cfx TmpNitCip	1				1				
Czl Tmp	1						1		
Czl Ctr Nit	1	1							
Czl Ctr TmpNit	1		1						
Czl Ctr Gen Nit	1								1
Czl CtrCaz Nit	1							1	
Czl CtrCaz TmpNitCip	1	1							
CzlCfx TmpNit	1						1		
Ptz CtrCaz NitCip	1							1	
PtzCzl Nit	1				1				
PtzCzl Caz NitCip	1		1						
Amc	1		1						
Amc Czl Nit	1				1				
Amc Czl CtrCaz TmpNit	1		1						
Amc Czl CtrCaz Gen TmpNitCip	1				1				
Amc CzlCfxCtr TmpNit	1		1						
Amc CzlCfxCtrCaz Gen TmpNitCipMer	1	1							
AmcPtzCzl TmpNit	1						1		
AmcPtzCzl Gen TmpNit	1							1	
AmcPtzCzl Ctr TmpNitCip	1				1				
AmcPtzCzl CtrCaz Gen TmpNitCip	1		1						
AmcPtzCzlCfx Nit	1						1		
AmcPtzCzlCfx TmpNit	1	1							
AmcPtzCzlCfxCtr Nit	1				1				
AmcPtzCzlCfxCtrCaz Nit	1	1							
AmcPtzCzlCfxCtrCaz Gen NitCip	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]									
TemShvCTXampC	AUS	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Escherichia coli (n=72)									
- - CTX -	27	2	6		5	4		6	4
Tem - CTX -	24		7	2	2	2	1	7	3
- - - ampC	6				2	2		2	
Tem - - -	5				1	1		1	2
- - - -	4				2			2	
Tem - - ampC	2		1					1	
TemShv - -	1							1	
(not received)	3							3	
Klebsiella oxytoca (n=4)									
- - - -	3		1					2	
(not received)	1							1	
Klebsiella pneumoniae (n=17)									
- ShvCTX -	6		2		1	1			2
TemShv - -	4	1	1		1			1	
TemShvCTX -	3		2					1	
- - CTX -	2			1	1				
- Shv - ampC	1				1				
- ShvCTXampC	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								7 (5.8)	19 (15.7)	14 (11.6)	34 (28.1)	47 (38.8)				121	33.1%	66.9%
co-amoxyclav								5 (4.1)	2 (1.6)	8 (6.6)	11 (9.0)	96 (78.7)				122	12.3%	87.7%
Ticarcillin/clavulanate										89 (73.0)	3 (2.5)	6 (4.9)	3 (2.5)	21 (17.2)		122	75.4%	24.6%
piperacillin/tazobactam									87 (71.3)	11 (9.0)		1 (0.8)	1 (0.8)	22 (18.0)		122	80.3%	19.7%
cefazolin									26 (21.3)	1 (0.8)			95 (77.9)			122	21.3%	78.7%
cefoxitin									6 (4.9)	1 (0.8)	3 (2.5)	3 (2.5)	109 (89.3)			122	5.7%	94.3%
ceftriaxone							95 (77.9)		4 (3.3)	3 (2.5)	10 (8.2)	2 (1.6)	8 (6.6)			122	77.9%	22.1%
ceftazidime							96 (78.7)		2 (1.6)	3 (2.5)	10 (8.2)	1 (0.8)	10 (8.2)			122	80.3%	19.7%
cefepime							121 (99.2)	1 (0.8)								122	100%	
gentamicin							121 (99.2)				1 (0.8)					122	99.2%	0.8%
tobramycin							121 (99.2)			1 (0.8)						122	99.2%	0.8%
amikacin								121 (99.2)	1 (0.8)							122	100%	
nalidixic acid								61 (50.0)	46 (37.7)	2 (1.6)	2 (1.6)	11 (9.0)				122	91.0%	9.0%
ciprofloxacin					115 (94.3)	3 (2.5)	1 (0.8)	1 (0.8)	2 (1.6)							122	97.5%	2.5%

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			
norfloxacin						107	3	9		2	1					122		
						(87.7)	(2.5)	(7.4)		(1.6)	(0.8)						97.5%	2.5%
trimethoprim						104	2	2	2	3	9					122		
						(85.2)	(1.6)	(1.6)	(1.6)	(2.5)	(7.4)						92.6%	7.4%
Trimethoprim/sulfa							111	6	2	1	2					122		
							(91.0)	(4.9)	(1.6)	(0.8)	(1.6)						95.9%	4.1%
meropenem					121		1									122		
					(99.2)		(0.8)										100%	
ertapenem[b]	11	18	32	22	17	13	3	3		1						120		
	(9.2)	(15.0)	(26.7)	(18.3)	(14.2)	(10.8)	(2.5)	(2.5)		(0.8)							94.2%	5.8%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek AST-N149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

[b] Ertapenem MICs performed by Etest strips (BioMerieux), 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								9 (6.6)	7 (5.1)	7 (5.1)	32 (23.4)	82 (59.9)				137	16.8%	83.2%
co-amoxyclav								8 (5.8)	8 (5.8)	3 (2.2)	6 (4.4)	112 (81.8)				137	13.9%	86.1%
Ticarcillin/clavulanate										86 (62.8)	11 (8.0)	5 (3.6)	4 (2.9)	31 (22.6)		137	70.8%	29.2%
piperacillin/tazobactam									89 (65.0)	16 (11.7)	5 (3.6)	2 (1.5)	2 (1.5)	23 (16.8)		137	80.3%	19.7%
cefazolin									8 (5.8)			1 (0.7)	128 (93.4)			137	5.8%	94.2%
cefoxitin									10 (7.3)	6 (4.4)		1 (0.7)	120 (87.6)			137	11.7%	88.3%
ceftriaxone							99 (72.3)	2 (1.5)	5 (3.6)	3 (2.2)	5 (3.6)	2 (1.5)	21 (15.3)			137	72.3%	27.7%
ceftazidime							98 (71.5)	2 (1.5)	6 (4.4)	5 (3.6)	3 (2.2)	2 (1.5)	21 (15.3)			137	77.4%	22.6%
cefepime							127 (92.7)	4 (2.9)	3 (2.2)	1 (0.7)	1 (0.7)		1 (0.7)			137	98.5%	1.5%
gentamicin							131 (95.6)				6 (4.4)					137	95.6%	4.4%
tobramycin							129 (94.2)			4 (2.9)	4 (2.9)					137	94.2%	5.8%
amikacin								130 (94.9)	3 (2.2)	1 (0.7)	3 (2.2)					137	100%	
nalidixic acid								62 (45.3)	49 (35.8)	10 (7.3)	5 (3.6)	11 (8.0)				137	92.0%	8.0%
ciprofloxacin					126 (92.0)	1 (0.7)	1 (0.7)	5 (3.6)	4 (2.9)							137	93.4%	6.6%
norfloxacin						121 (88.3)	1 (0.7)	8 (5.8)	2 (1.5)	3 (2.2)	2 (1.5)					137	96.4%	3.6%

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						81 (59.1)	21 (15.3)	8 (5.8)	4 (2.9)	1 (0.7)	22 (16.1)					137	83.9%	16.1%
Trimethoprim/sulfa							112 (81.8)	3 (2.2)	1 (0.7)		21 (15.3)					137	83.9%	16.1%
meropenem					136 (99.3)	1 (0.7)										137	100%	
ertapenem[b]	23 (16.9)	22 (16.2)	16 (11.8)	17 (12.5)	19 (14.0)	17 (12.5)	15 (11.0)	6 (4.4)	1 (0.7)							136	83.8%	16.2%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek AST-N149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

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

Escherichia coli

Drug	0.016	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	Total	%S	%IR
	Number (percentage) of Minimum Inhibitory Concentrations (mg/L) at: [a]																	
ampicillin								802 (38.3)	243 (11.6)	112 (5.4)	28 (1.3)	907 (43.4)				2092	55.3%	44.7%
co-amoxyclav								676 (32.3)	690 (33.0)	287 (13.7)	310 (14.8)	129 (6.2)				2092	79.0%	21.0%
Ticarcillin/clavulanate										1376 (65.8)	470 (22.5)	88 (4.2)	63 (3.0)	95 (4.5)		2092	88.2%	11.8%
piperacillin/tazobactam									1962 (93.8)	44 (2.1)	17 (0.8)	2 (0.1)	8 (0.4)	59 (2.8)		2092	96.7%	3.3%
cefazolin									1773 (84.8)	42 (2.0)	134 (6.4)	9 (0.4)	134 (6.4)			2092	84.8%	15.2%
cefoxitin									1944 (92.9)	62 (3.0)	49 (2.3)	15 (0.7)	22 (1.1)			2092	95.9%	4.1%
ceftriaxone							2026 (96.8)		2 (0.1)	4 (0.2)	3 (0.1)	6 (0.3)	51 (2.4)			2092	96.8%	3.2%
ceftazidime							2034 (97.2)	2 (0.1)	17 (0.8)	2 (0.1)	28 (1.3)		9 (0.4)			2092	98.1%	1.9%
cefepime							2045 (97.8)	15 (0.7)	8 (0.4)	10 (0.5)		2 (0.1)	12 (0.6)			2092	99.3%	0.7%
gentamicin							1920 (91.8)	54 (2.6)	26 (1.2)	5 (0.2)	87 (4.2)					2092	95.6%	4.4%
tobramycin							1957 (93.5)	32 (1.5)	14 (0.7)	60 (2.9)	29 (1.4)					2092	95.7%	4.3%
amikacin								1616 (77.2)	404 (19.3)	37 (1.8)	34 (1.6)		1 (0.0)			2092	100%	
nalidixic acid								1632 (78.0)	201 (9.6)	22 (1.1)	10 (0.5)	227 (10.9)				2092	89.1%	10.9%
ciprofloxacin					1900 (90.8)	66 (3.2)	14 (0.7)	4 (0.2)	108 (5.2)							2092	94.6%	5.4%
norfloxacin						1877 (89.7)	20 (1.0)	84 (4.0)	3 (0.1)	6 (0.3)	102 (4.9)					2092	94.8%	5.2%

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						1607 (76.8)	14 (0.7)	4 (0.2)	4 (0.2)	20 (1.0)	443 (21.2)					2092	78.8%	21.2%
Trimethoprim/sulfa							1656 (79.2)	23 (1.1)	1 (0.0)	3 (0.1)	409 (19.6)					2092	80.2%	19.8%
meropenem					2092 (100)											2092	100%	
ertapenem[b]	1941 (93.2)	102 (4.9)	12 (0.6)	9 (0.4)	10 (0.5)	7 (0.3)	2 (0.1)									2091	99.9%	0.1%

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[b] Ertapenem MICs performed by Etest strips (BioMerieux), 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									1 (1.0)	1 (1.0)	28 (27.7)	71 (70.3)				101	2.0%	98.0%
co-amoxyclav								56 (55.4)	26 (25.7)	10 (9.9)	4 (4.0)	5 (5.0)				101	91.1%	8.9%
Ticarcillin/clavulanate										92 (91.1)	3 (3.0)	1 (1.0)	2 (2.0)	3 (3.0)		101	94.1%	5.9%
piperacillin/tazobactam									91 (90.1)	1 (1.0)	2 (2.0)			7 (6.9)		101	93.1%	6.9%
cefazolin									32 (31.7)	25 (24.8)	10 (9.9)	3 (3.0)	31 (30.7)			101	31.7%	68.3%
cefoxitin									93 (92.1)	3 (3.0)	3 (3.0)	1 (1.0)	1 (1.0)			101	95.0%	5.0%
ceftriaxone							97 (96.0)	1 (1.0)	1 (1.0)		2 (2.0)					101	96.0%	4.0%
ceftazidime							100 (99.0)		1 (1.0)							101	100%	
cefepime							100 (99.0)	1 (1.0)								101	100%	
gentamicin							101 (100)									101	100%	
tobramycin							101 (100)									101	100%	
amikacin								98 (97.0)	3 (3.0)							101	100%	
nalidixic acid								71 (70.3)	20 (19.8)	3 (3.0)	3 (3.0)	4 (4.0)				101	96.0%	4.0%
ciprofloxacin					96 (95.0)	3 (3.0)	1 (1.0)		1 (1.0)							101	99.0%	1.0%
norfloxacin						97 (96.0)	1 (1.0)	2 (2.0)		1 (1.0)						101	99.0%	1.0%

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						89 (88.1)	2 (2.0)		3 (3.0)	1 (1.0)	6 (5.9)					101	94.1%	5.9%
Trimethoprim/sulfa							94 (93.1)	2 (2.0)			5 (5.0)					101	95.0%	5.0%
meropenem					101 (100)											101	100%	
ertapenem[b]	91 (91.9)	7 (7.1)			1 (1.0)											99	100%	

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b Ertapenem MICs performed by Etest strips (BioMerieux), 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								9 (1.9)	4 (0.8)	10 (2.1)	161 (33.9)	291 (61.3)				475	4.8%	95.2%
co-amoxyclav								337 (70.9)	80 (16.8)	36 (7.6)	11 (2.3)	11 (2.3)				475	95.4%	4.6%
Ticarcillin/clavulanate										428 (90.1)	27 (5.7)	8 (1.7)	1 (0.2)	11 (2.3)		475	95.8%	4.2%
piperacillin/tazobactam									427 (89.9)	22 (4.6)	8 (1.7)	3 (0.6)		15 (3.2)		475	96.2%	3.8%
cefazolin									443 (93.3)	2 (0.4)	1 (0.2)	1 (0.2)	28 (5.9)			475	93.3%	6.7%
cefoxitin									430 (90.5)	25 (5.3)	7 (1.5)	5 (1.1)	8 (1.7)			475	95.8%	4.2%
ceftriaxone							459 (96.6)			2 (0.4)	2 (0.4)	3 (0.6)	9 (1.9)			475	96.6%	3.4%
ceftazidime							464 (97.7)		2 (0.4)		4 (0.8)		5 (1.1)			475	98.1%	1.9%
cefepime							467 (98.3)	3 (0.6)	2 (0.4)	3 (0.6)						475	100%	
gentamicin							464 (97.7)				11 (2.3)					475	97.7%	2.3%
tobramycin							460 (96.8)	2 (0.4)	1 (0.2)	9 (1.9)	3 (0.6)					475	97.5%	2.5%
amikacin								470 (98.9)	3 (0.6)		1 (0.2)		1 (0.2)			475	99.8%	0.2%
nalidixic acid								284 (59.8)	121 (25.5)	21 (4.4)	8 (1.7)	41 (8.6)				475	91.4%	8.6%
ciprofloxacin					436 (91.8)	15 (3.2)	13 (2.7)	1 (0.2)	10 (2.1)							475	97.7%	2.3%
norfloxacin						427 (89.9)	2 (0.4)	36 (7.6)		1 (0.2)	9 (1.9)					475	97.9%	2.1%

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						383 (80.6)	11 (2.3)	5 (1.1)	15 (3.2)	11 (2.3)	50 (10.5)					475	89.5%	10.5%
Trimethoprim/sulfa							412 (86.7)	21 (4.4)	2 (0.4)	1 (0.2)	39 (8.2)					475	91.2%	8.8%
meropenem					472 (99.4)	1 (0.2)	1 (0.2)	1 (0.2)								475	99.8%	0.2%
ertapenem[b]	331 (70.0)	92 (19.5)	36 (7.6)	9 (1.9)	1 (0.2)	2 (0.4)	1 (0.2)	1 (0.2)								473	99.6%	0.4%

[a] Shaded areas indicate ≤ and ≥ MIC values available on the Vitek AST-N149 card; vertical lines indicate CLSI M100-S22 susceptible (blue) and resistant (red) breakpoints.

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