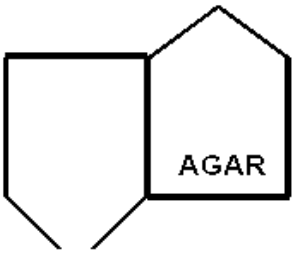

The Australian Group on Antimicrobial Resistance

Gram-negative Survey

2006 Antimicrobial Susceptibility Report

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

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2 EXECUTIVE SUMMARY

The Australian Group on Antimicrobial Resistance (AGAR) performs regular multicentre period-prevalence studies to monitor changes in antimicrobial resistance. In 2006, 31 laboratories from each state and mainland territory of Australia participated in national surveillance of selected Gram negative genera of particular clinical importance, which were collected prospectively from clinically significant specimens. Seven hundred and sixty two *E. coli*, 750 *Enterobacter* sp, 712 *Klebsiella* sp and 334 *Acinetobacter* sp were tested using a commercial automated method (Vitek 2). Results were analysed using CLSI break points from 2010. Forty percent of isolates came from urinary tract specimens, while 20% and 16% of isolates came from blood and wounds respectively.

In *E. coli* moderate to high levels of resistance were demonstrated for ampicillin (48%), amoxicillin-clavulanate (17%), cephalothin (42%), cefazolin (15%) and trimethoprim (20%). Resistance was uncommon (<5%) for ticarcillin-clavulanate, piperacillin-tazobactam, ceftriaxone, ceftazidime, gentamicin and ciprofloxacin. No strains resistant to cefepime or meropenem were seen in the 2006 survey.

Klebsiella species demonstrated higher levels of resistance compared with *E. coli* for piperacillin-tazobactam (2.4%), cefazolin (22%), ceftriaxone (5.6%), ceftazidime (2.5%), but lower levels of resistance for cephalothin (12%), ciprofloxacin (2.5%), gentamicin (2.8%) and trimethoprim (7.0%). In general, *K. oxytoca* was more resistant than *K. pneumoniae*. Small numbers of *Klebsiella* isolates were resistant to cefepime or meropenem, reflected extended spectrum ß-lactamase or carbapenemase production.

High rates of resistance to third generation cephalosporins and ticarcillin-clavulanate were demonstrated in *Enterobacter* sp, indicative of de-repression of intrinsic chromosomal ß-lactamase production, but this was much lower for piperacillin – tazobactam. Resistance to cefepime and meropenem (suggesting extended-spectrum ß-lactamase or carbapenemase production) were very low (<1%). Resistance to non ß-lactam agents were low to moderate; ciprofloxacin (3.3%), gentamicin (6.3%), trimethoprim (12.5%).

Of the genera tested, the highest resistant rates were demonstrated in *Acinetobacter* sp with significant resistance to ß-lactam agents including cefepime (20%) and meropenem (18%) as well as ciprofloxacin (29%) and gentamicin (24%).

In this survey tigecycline was tested for the first time. This is a new intravenous agent, from the tetracycline class, with broad spectrum activity against Gram positive and Gram negative bacteria. The small number of resistant isolates seen is concerning but further work is required to ensure this reflects true resistance rather than a methodological error.

The major resistance problem in Gram negatives, is multi-resistance, as treatment (if any is available) is limited to less effective, more toxic and more expensive agents. Usually there are no effective oral antibiotic options. Nosocomial outbreaks of multiresistant organisms are increasingly reported worldwide including in Australia. This is especially so with outbreaks of multiresistant *Acinetobacter* and this is reflected in the high resistance rates seen in this genera in this study. While rates of multi-resistance are lower in the Enterobacteriaciae than in *Acinetobacter* species, they are more problematic because of their higher virulence and propensity to cause community as well as nosocomial infections.

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. The objectives of the 2006 surveillance program were:

1. Determine proportions of resistance to the main therapeutic agents in *Escherichia coli*, *Klebsiella* species, *Enterobacter* species and *Acinetobacter* species in Australian institutions
2. Examine the extent of co-resistance and multi-resistance in these species
3. Detect emerging resistance to 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.

Escherichia 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 multiresistant. They acquire resistance to important Gram-negative agents relatively easily.

Acinetobacter species are strongly associated with infections in critical care patients, and other forms of nosocomial infection to a lesser extent. The species have both human and environmental reservoirs. The commonest members of the genus, the *Acinetobacter baumannii* complex, harbour intrinsic resistance to aminopenicillins, ß-lactamase inhibitor combinations, first and second generation cephalosporins and aztreonam. The also have a high capacity to acquire further resistances.

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]

Cephalothin and cefazolin: first-generation cephalosporins; cephalothin used to predict cephalexin for urinary tract infection. Cephalothin no longer considered to have useful systemic activity against Enterobacteriaceae. Cefazolin

is an important agent for surgical prophylaxis and penicillin-allergic patients. [Parenteral, cephalexin oral, 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 the other carbapenems, imipenem and ertapenem, 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.

Tigecycline: a glycylcycline. A new class of antibiotics derived from tetracycline. These tetracycline analogues are specifically designed to overcome two common mechanisms of tetracycline resistance, namely resistance mediated by acquired efflux pumps and/or ribosomal protection. Used as a reserve agent for multiresistant organisms.

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 e.g. cefoxitin) and third generation cephalosporins, monobactam	Mainly hospital-associated until recent emergence in community practice overseas
K1 hyperproduction	*K. oxytoca*	Ampicillin, amoxicillin, piperacillin, first- and second-generation cephalosporins, aztreonam, ceftriaxone > cefotaxime	Natural enzyme selected to hyperproduction
Chromosomal cephalosporinases	ESCaPPM*	Ampicillin, amoxicillin, first-, second-generation cephalosporins, third generation cephalosporins in de-repressed mutants.	Natural enzymes. Selection for stably de-repressed mutants can occur during treatment and strains with this are common
Plasmid-borne AmpC ß-lactamases	*E. coli, K. pneumoniae*	Ampicillin, amoxycillin, first, second and third-generation cephalosporins, including cephamycins	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.

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 one institutions from each State and mainland Territories of Australia participated in the Gram-negative 2006 AGAR survey. Each institution collected up to 25 *E. coli*, 25 *Klebsiella* species, 25 *Enterobacter* species and 25 *Acinetobacter* (non *A. lwoffii*) species from different patients. The following limits were placed on specimen types for *E. coli* and *Klebsiella* species in order to maximize the number of isolates from more serious infections, such as bacteraemia:

Catheter urine (CSU) ≤ 5

Non-catheter urine ≤ 7
Tracheal aspirate ≤ 5
Wounds ≤ 5
Expectorated sputum ≤ 2

There was no limit for blood or sterile body site specimens (pleural fluid, CSF, peritioneal dialysate).

Institutions collected consecutive clinically significant *Enterobacter* and *Acinetobacter* species without specimen type limits.

Table 2. Isolates Tested

Region	Number of Institutions	*E. coli*	*Enterobacter* species	*Klebsiella* species	*Acinetobacter* species	Total
New South Wales (NSW) Australian Capital Territory (ACT)	9	223	226	215	99	763
Northern Territory (NT) Queensland (QLD)	6	150	151	147	104	552
South Australia (SA)	4	99	77	79	37	292
Victoria (VIC) Tasmania (TAS)	8	190	197	173	52	612
Western Australia (WA)	4	100	99	98	42	339
Total	**31**	**762**	**750**	**712**	**334**	**2558**

4.1 PARTICIPATING INSTITUTIONS

ACT/NSW (9)
Concord Hospital
Douglass Hanly Moir
John Hunter Hospital
Nepean Hospital
Royal North Shore Hospital
Royal Prince Alfred Hospital
Sydney South West Pathology Services
The Canberra Hospital
Westmead Hospital

QLD/NT (6)
Pathology Queensland, Gold Coast Hospital
Pathology Queensland, Prince Charles Hospital
Pathology Queensland, Princess Alexandra Hospital
Pathology Queensland, Central Laboratory
Royal Darwin Hospital
Sullivan Nicolaides Pathology

SA (4)
SA Pathology (Flinders Medical Centre)
Gribbles Pathology
SA Pathology (Royal Adelaide Hospital)
SA Pathology (Women's and Children's Hospital)

VIC/TAS (8)

Alfred Hospital
Austin Health
Gribbles Pathology
Launceston General Hospital
Monash Medical Centre
Royal Children's Hospital
Royal Hobart 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

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

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

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

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

Acinetobacter spp. (saccharolytic) – non *A. lwoffi* (non-saccharolytic)

API20NE
MicroScan®
Vitek® or Phoenix Automated Microbiology System
Agar replication
Browning effect on Columbia Horse Blood D-glucose Agar

4.2.2 MOLECULAR METHODS

All referred isolates were screened for the presence of the *bla*TEM and *bla*SHV genes using previously reported oligonucleotide primers. A multiplex real-time TaqMan PCR was used to detect CTX-M-type genes (Birkett et al J Med Micro (2007) 56; 52). Strains were probed for plasmid-borne AmpC enzymes using the method described by Pérez-Pérez et al. (J Clin Microbiol.(2002) 40:2153-2162). Allele-specifi c PCR for the *pabB* gene was used to screen strains of *E. coli* belonging to ST131 and potentially pathogenic *E. coli* groups were determined using the methods described by Clermont et.al. (JAC (2009) 64:274; Appl. Environ. Microbiol. (2000) 66:4555).

4.2.3 SPECIES INCLUDED IN STUDY

Table 3. Species included

Group	Organism	Total
E. coli	*E. coli*	762
Enterobacter	*E. cloacae*	500
	E. aerogenes	230
	E. asburiae	7
	Enterobacter spp.	5
	E. amnigeneus	2
	E. sakazakii	2
	E. cancerogenus	2
	E. intermedius	1
	E. gergoviae	1
	Total	750
Klebsiella	*K. pneumoniae*	499
	K. oxytoca	199
	Klebsiella spp.	11
	K. ozaenae	3
	Total	712
Acinetobacter	*A. baumannii*	314
	Acinetobacter spp.	17
	A. haemolyticus	3
	Total	334

4.3 SUSCEPTIBILITY TESTING

4.3.1 METHOD

Testing was performed by the CLSI and EUCAST standard method of broth microdilution. Commercially available Vitek AST-N044 cards were utilized by all participants throughout the survey period. The most recent CLSI breakpoints from January 2010 have been employed in the analysis

4.3.2 ANTIBIOTICS TESTED

Table 4. Antimicrobials Tested

Antimicrobial Agent		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	≤1	2	≥4
Cephalothin		≤2, 4, 8, 16, 32, ≥64	≤8	16	≥32
Cefepime		≤1, 2, 4, 8, 16, 32, ≥64	≤8	16	≥32
Ceftriaxone	**Enterobacteriaceae**	≤1, 2, 4, 8, 16, 32, ≥64	≤1	2	≥4

	***Acinetobacter* spp.**	≤1, 2, 4, 8, 16, 32, ≥64	≤8	16-32	≥64
Cefoxitin		≤4, 8, 16, 32, ≥64	≤8	16	≥32
Ceftazidime[c]	**Enterobacteriaceae**	≤1, 2, 4, 8, 16, 32, ≥64	≤4	8	≥16
	***Acinetobacter* spp.**	≤1, 2, 4, 8, 16, 32, ≥64	≤8	16	≥32
Meropenem[d]	**Enterobacteriaceae**	≤0.25, 0.5, 1, 2, 4, 8, ≥16	≤1	2	≥4
	***Acinetobacter* spp.**	≤0.25, 0.5, 1, 2, 4, 8, ≥16	≤4	8	≥16
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
Tigecycline[e]		≤0.5, 1, 2, 4, ≥8	≤2	4	≥8

[a] The breakpoints selected to determine resistance are described in Performance Standards for Antimicrobial Susceptibility Testing: Twentieth Information Supplement, CLSI document M100-S20, January 2010.
[b] For cefazolin, breakpoints of ≤1, 2, ≥4 are still under discussion. For analysis, breakpoints of ≤4, ≥8 were appied due to the MIC range available on the Vitek card
[c] Published new CLSI breakpoints
[d] Proposed new CLSI breapoints
[e] For tigecycline, FDA breakponts

4.4 QUALITY CONTROL

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

5 SOURCE OF ISOLATES

The majority of isolates were from urine. Twenty percent were from blood cultures. Over one third of the *E. coli* isolates were from blood cultures, with lower percentages for *Klebsiella* and *Enterobacter* species. Other sites of isolation reflect the high incidence of these species in nosocomial and pre- and post-operative surgical infections.

Table 5. Source of Isolates

Specimen	*E. coli*		Enterobacter		Klebsiella		Acinetobacter		Total	
Urine -other	196	25.7%	320	42.7%	203	28.5%	90	26.9%	809	31.6%
Blood	262	34.4%	56	7.5%	175	24.6%	24	7.2%	517	20.2%
Catheter urine	85	11.2%	61	8.1%	85	11.9%	22	6.6%	253	9.9%
Wound	84	11.0%	148	19.7%	89	12.5%	84	25.1%	405	15.8%
Other	24	3.1%	24	3.2%	17	2.4%	21	6.3%	86	3.4%
Respiratory	26	3.4%	54	7.2%	42	5.9%	47	14.1%	169	6.6%
Sterile Site	60	7.9%	37	4.9%	53	7.4%	11	3.3%	161	6.3%
Tracheal Aspirate	24	3.1%	46	6.1%	44	6.2%	34	10.2%	148	5.8%
IV Line Tip	1	0.1%	4	0.5%	4	0.6%	1	0.3%	10	0.4%
Total	**762**	**100.0%**	**750**	**100.0%**	**712**	**100.0%**	**334**	**100.0%**	**2558**	**100.0%**

6 SUSCEPTIBILITY TESTING RESULTS

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

6.1 PERCENTAGES RESISTANT/NON-SUSCEPTIBLE

Table 6. Ampicillin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	52.0%	42.7%	39.4%	51.6%	49.0%	48.0%
***Enterobacter* spp.**	%R	60.2%	64.2%	57.1%	62.9%	49.5%	60.0%
E. cloacae	%R	68.4%	70.0%	64.6%	66.9%	48.2%	65.8%
E. aerogenes	%R	42.9%	48.0%	45.8%	56.5%	50.0%	49.1%
***Klebsiella* spp.**	%R	69.3%	74.1%	79.7%	68.2%	71.4%	71.5%
K. pneumoniae	%R	67.4%	72.2%	80.4%	63.8%	69.5%	69.1%
K. oxytoca	%R	74.3%	80.8%	76.0%	80.0%	73.7%	76.4%

Comments: Resistance to ampicillin is intrinsic in *Klebsiella* and *Enterobacter* species, due to natural ß-lactamases.

Table 7. Amoxycillin-clavulanate

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%I	10.3%	11.3%	7.1%	14.7%	15.0%	11.8%
	%R	6.3%	4.0%	4.0%	5.3%	7.0%	5.4%
***Enterobacter* spp.**	%I	5.8%	5.3%	7.8%	4.6%	6.1%	5.6%
	%R	85.4%	84.8%	83.1%	82.2%	76.8%	83.1%
E. cloacae	%I	6.6%	5.8%	8.3%	3.2%	8.9%	6.0%
E. cloacae	%R	85.5%	85.8%	87.5%	83.1%	64.3%	82.8%
E. aerogenes	%I	4.3%	4.0%	8.3%	7.2%	2.4%	5.2%
E. aerogenes	%R	85.7%	84.0%	79.2%	79.7%	92.9%	84.3%
***Klebsiella* spp.**	%I	1.9%	7.5%	1.3%	4.0%	2.0%	3.5%
	%R	4.7%	2.0%	2.5%	1.7%	3.1%	2.9%
K. pneumoniae	%I	0.7%	4.3%	0.0%	3.1%	1.7%	2.2%
K. pneumoniae	%R	4.9%	1.7%	2.0%	1.5%		2.4%
K. oxytoca	%I	4.3%	19.2%	4.0%	4.0%	7.5%	6.5%
K. oxytoca	%R	4.3%	3.8%	4.0%	2.5%	7.9%	4.5%

Comments: Intermediate susceptibility or resistance to amoxycillin-clavulanate is intrinsic in *Enterobacter* species, due to natural ß-lactamases. Intermediate susceptibility is common in *E. coli* due to hyperproduction of acquired ß-lactamases, and in *Klebsiella* species due to higher levels of natural ß-lactamases.

Table 8. Ticarcillin-clavulanate

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	39.4%	26.9%	18.9%	9.6%	2.4%	24.0%
E. coli	%R	2.7%	6.0%	3.0%	3.7%	5.0%	3.9%
***Enterobacter* spp.**	%R	30.5%	17.2%	28.6%	28.9%	14.1%	25.1%
E. cloacae	%R	31.6%	17.5%	25.0%	28.2%	8.9%	24.2%
E. aerogenes	%R	30.0%	16.0%	37.5%	30.4%	21.4%	27.8%
***Klebsiella* spp.**	%R	5.1%	3.4%	1.3%	2.9%	4.1%	3.7%
K. pneumoniae	%R	4.2%	2.6%	0.0%	3.1%	0.0%	2.6%
K. oxytoca	%R	7.1%	7.7%	4.0%	2.5%	10.5%	6.5%

Comments: Resistance to ticarcillin-clavulanate may indicate the presence of AmpC ß-lactamases.

Table 9. Piperacillin-tazobactam

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	35.4%	26.0%	0.0%	0.0%	0.0%	18.6%
E. coli	%R	0.0%	0.7%	0.0%	0.0%	2.0%	0.4%
***Enterobacter* spp.**	%R	3.1%	6.6%	6.5%	6.6%	1.0%	4.8%
E. cloacae	%R	4.6%	8.3%	8.3%	8.9%	1.8%	6.6%
E. aerogenes	%R	0.0%	0.0%	4.2%	2.9%	0.0%	1.3%
***Klebsiella* spp.**	%R	3.3%	3.4%	1.3%	1.2%	2.0%	2.4%
K. pneumoniae	%R	1.4%	0.9%	0.0%	0.0%	0.0%	0.6%
K. oxytoca	%R	7.1%	15.4%	4.0%	5.0%	5.3%	7.0%

Comments: Resistance to piperacillin-tazobactam may indicate the presence of AmpC ß-lactamases.

Table 10. Cephalothin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%I	34.5%	28.0%	17.2%	26.8%	31.0%	28.6%
	%R	12.1%	11.3%	16.2%	15.8%	15.0%	13.8%
Enterobacter spp.	%I	11.1%	6.6%	5.2%	6.1%	11.1%	8.3%
	%R	85.8%	92.1%	90.9%	89.3%	86.9%	88.7%
Klebsiella spp.	%I	3.7%	3.4%	1.3%	3.5%	1.0%	2.9%
	%R	11.2%	8.8%	7.6%	8.1%	5.1%	8.7%

Comments: The activity of cephalothin against *E. coli* is naturally marginal (wild-type MIC values straddle the susceptible breakpoint. Hence there is a naturally high rate of intermediate susceptibility in this species). *Enterobacter* species are intrinsically resistant due to natural ß-lactamases. Cephalothin susceptibility results are used to predict cephalexin susceptibility for urinary isolates.

Table 11. Cefazolin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	13.5%	12.0%	16.2%	14.2%	20.0%	14.6%
***Enterobacter* spp.**	%R	92.5%	94.7%	97.4%	93.9%	93.9%	94.0%
E. cloacae	%NS	97.4%	98.3%	100.0%	94.4%	92.9%	96.6%
E. aerogenes	%NS	82.9%	84.0%	91.7%	92.8%	95.2%	89.1%
***Klebsiella* spp.**	%R	23.3%	17.7%	22.8%	21.4%	27.6%	22.2%
K. pneumoniae	%NS	11.1%	7.0%	5.9%	8.5%	6.8%	8.4%
K. oxytoca	%NS	48.6%	65.4%	60.0%	65.0%	60.5%	57.8%

Comments:
Interpretation based on MIC range available on Vitek card.
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 12. Ceftriaxone

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	43.4%	27.9%	21.6%	9.6%	2.4%	25.7%
E. coli	%NS	3.6%	1.3%	4.0%	2.1%	2.0%	2.6%
***Enterobacter* spp.**	%NS	35.8%	24.5%	33.8%	38.6%	20.2%	32.0%
E. cloacae	%NS	37.5%	25.8%	39.6%	35.5%	24.3%	31.8%
E. aerogenes	%NS	34.3%	20.0%	29.2%	44.9%	28.6%	34.3%
***Klebsiella* spp.**	%NS	7.9%	5.4%	3.8%	5.2%	3.1%	5.6%
K. pneumoniae	%NS	6.3%	2.6%	3.9%	4.6%	1.7%	4.2%
K. oxytoca	%NS	11.4%	15.4%	4.0%	7.5%	5.3%	9.0%

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

Table 13. Ceftazidime

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	41.4%	26.9%	18.9%	7.7%	4.8%	24.6%
E. coli	%NS	2.2%	0.7%	0.0%	1.6%	2.0%	1.4%
***Enterobacter* spp.**	%NS	35.0%	21.9%	32.5%	34.0%	15.2%	29.2%
E. cloacae	%NS	35.8%	22.5%	35.4%	29.0%	8.9%	27.9%
E. aerogenes	%NS	33.3%	20.0%	33.3%	43.5%	23.8%	33.2%
***Klebsiella* spp.**	%NS	4.7%	0.7%	2.5%	2.3%	1.0%	2.5%
K. pneumoniae	%NS	5.6%	0.0%	3.9%	3.1%	1.7%	3.0%
K. oxytoca	%NS	2.9%	3.8%	0.0%	0.0%	0.0%	1.5%

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

Table 14. Cefepime

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	38.4%	23.1%	0.0%	7.7%	0.0%	19.8%
E. coli	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Enterobacter* spp.**	%NS	0.0%	0.0%	3.9%	1.0%	0.0%	0.7%
E. cloacae	%NS	0.0%	0.0%	4.2%	0.8%	0.0%	0.6%
E. aerogenes	%NS	0.0%	0.0%	4.2%	1.4%	0.0%	0.9%
***Klebsiella* spp.**	%NS	2.3%	0.0%	0.0%	1.2%	0.0%	1.0%
K. pneumoniae	%NS	3.5%	0.0%	0.0%	1.5%	0.0%	1.4%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

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

Table 15. Meropenem

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	35.4%	24.0%	0.0%	0.0%	0.0%	18.0%
E. coli	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
***Enterobacter* spp.**	%NS	0.4%	0.7%	2.6%	0.0%	0.0%	0.5%
E. cloacae	%NS	0.7%	0.8%	2.1%	0.0%	0.0%	0.6%
E. aerogenes	%NS	0.0%	0.0%	4.2%	0.0%	0.0%	0.4%
***Klebsiella* spp.**	%NS	0.0%	0.0%	0.0%	0.6%	0.0%	0.1%
K. pneumoniae	%NS	0.0%	0.0%	0.0%	0.8%	0.0%	0.2%
K. oxytoca	%NS	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

Comments: Resistance in Enterobacteriaceae indicates the presence of carbapenemases.

Table 16. Ciprofloxacin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	49.5%	30.8%	21.6%	9.6%	4.8%	28.7%
E. coli	%NS	6.7%	2.0%	6.1%	4.7%	4.0%	4.9%
***Enterobacter* spp.**	%NS	5.3%	1.3%	3.9%	2.5%	3.0%	3.3%
E. cloacae	%NS	7.2%	1.7%	0.0%	3.2%	1.8%	3.6%
E. aerogenes	%NS	1.4%	0.0%	4.2%	1.4%	4.8%	2.2%
***Klebsiella* spp.**	%NS	3.7%	3.4%	2.5%	1.2%	1.0%	2.5%
K. pneumoniae	%NS	5.6%	3.5%	3.9%	1.5%	0.0%	3.2%
K. oxytoca	%NS	0.0%	3.8%	0.0%	0.0%	2.6%	1.0%

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

Table 17. Gentamicin

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
***Acinetobacter* spp.**	%R	36.4%	26.9%	18.9%	11.5%	4.8%	23.7%
E. coli	%R	6.7%	2.0%	7.1%	4.2%	1.0%	4.5%
***Enterobacter* spp.**	%R	11.5%	6.6%	7.8%	2.5%	0.0%	6.3%
E. cloacae	%R	15.8%	8.3%	12.5%	3.2%	0.0%	8.8%
E. aerogenes	%R	2.9%	0.0%	0.0%	1.4%	0.0%	1.3%
***Klebsiella* spp.**	%R	3.7%	3.4%	1.3%	2.9%	1.0%	2.8%
K. pneumoniae	%R	4.9%	2.6%	2.0%	3.1%	1.7%	3.2%
K. oxytoca	%R	1.4%	3.8%	0.0%	2.5%	0.0%	1.5%

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

Table 18. Trimethoprim

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%R	22.9%	16.7%	16.2%	20.0%	19.0%	19.6%
***Enterobacter* spp.**	%R	17.3%	12.6%	18.2%	10.2%	2.0%	12.5%
E. cloacae	%R	21.7%	15.0%	14.6%	14.5%	1.8%	15.4%
E. aerogenes	%R	8.6%	0.0%	20.8%	2.9%	2.4%	6.1%
***Klebsiella* spp.**	%R	7.4%	10.2%	11.4%	4.6%	2.0%	7.0%
K. pneumoniae	%R	8.3%	10.4%	15.7%	4.6%	1.7%	7.8%
K. oxytoca	%R	5.7%	7.7%	4.0%	5.0%	2.6%	5.0%

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

Table 19. Tigecycline

Species		NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	%NS	0.4%	0.0%	0.0%	0.0%	0.0%	0.1%
***Enterobacter* spp.**	%NS	1.3%	3.3%	2.6%	5.6%	1.0%	2.9%
E. cloacae	%NS	1.3%	3.3%	2.1%	6.5%	1.8%	3.2%
E. aerogenes	%NS	1.4%	4.0%	0.0%	4.3%	0.0%	2.2%
***Klebsiella* spp.**	%NS	4.2%	2.7%	1.3%	1.2%	0.0%	2.2%
K. pneumoniae	%NS	5.6%	2.6%	2.0%	1.5%	0.0%	2.8%
K. oxytoca	%NS	1.4%	3.8%	0.0%	0.0%	0.0%	1.0%

Comments: Tigecycline resistance usually indicates the overexpression of AcrAB, a member of the RND multidrug efflux family. Susceptibility results were strongly influenced by the brand of testing medium used, and influenced the results in the Table. The results represent the percentages non-susceptible from the pooled results. Further work is required to determine whether these percentages represent true resistance or the result of methodology problems.

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, with the exception of NSW/ACT, which has higher percentages of acquired resistance to many drug classes in *Enterobacter* species compared to the other states. Furthermore, isolates causing bacteraemia had similar percentages of resistance to isolates from other specimen sources.

E. coli

Ampicillin resistance proportions have been high for more than a decade, and approximately stable at around 48%. 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* and *Klebsiella* spp. Cephalothin has always had fairly marginal activity against *E. coli;* its susceptibility results are used to predict cephalexin susceptibility for urinary isolates. Moderate levels of non-susceptibility have persisted for some years. Cefazolin maintains modest levels of resistance. Ciprofloxacin resistance appears to be increasing despite controlled usage in both the community and in hospitals. Gentamicin resistance remains fairly low despite more three decades of use in hospital practice. Trimethoprim, especially as cotrimoxazole, use has been high in the community and this is reflected in the resistance percentages.

***Klebsiella* species**

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 first generation cephalosporins cephalothin and cefazolin. Resistance to gentamicin is still low. Surprisingly, resistance to ciprofloxacin and trimethoprim is less common than in *E. coli*.

***Enterobacter* species**

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

6.3 MAJOR RESISTANCES

6.3.1 ESBLS

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

Most ESBL-producing strains will be captured/recognised using the new CLSI ceftriaxone breakpoints (≥ 1 mg/L). The ceftazidime breakpoints apply to clinical interpretation, but lower concentrations are required to identifying ESBL producers. The usual screening concentration of ceftazidime used for this purpose is 1 mg/L. Neither of these test agents will identify ESBL production in *Enterobacter* species because of their chromosomal AmpC ß-lactamase. Instead, cefepime at 1 mg/L is a reasonable indicator that an isolate of this genus habours an ESBL.

Table 20. Presumptive/Confirmed Extended-spectrum ß-lactamase Production

Species	NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
Escherichia coli	10	2	4	5	2	23
Ceftriaxone > 1 mg/L	3.6%	1.3%	4.0%	2.1%	2.0%	2.6%
Ceftazidime > 1 mg/L	3.6%	0.7%	1.0%	2.6%	2.0%	2.2%
Either of above	4.5%	1.3%	4.0%	2.6%	2.0%	3.0%
Confirmed						
any ESBL (No. received)	3/4	2/2	2/2	3/4	2/2	12/14
CTX-M types	1	1	1	2	0	5
plasmid-borne AmpC	0	0	1	0	2	3
Klebsiella pneumoniae	9	3	2	6	1	21
Ceftriaxone > 1 mg/L	6.3%	2.6%	3.9%	4.6%	1.7%	4.2%
Ceftazidime > 1 mg/L	6.3%	1.7%	3.9%	3.8%	1.7%	3.8%
Either of above	6.3%	2.6%	3.9%	4.6%	1.7%	4.2%
Confirmed						
any ESBL (No. received)	6/6	3/3	2/2	5/5	1/1	17/17
CTX-M types	3	1	1	3	0	8
plasmid-borne AmpC	0	0	0	1	1	2
Klebsiella oxytoca	9	4	1	3	2	19
Ceftriaxone > 1 mg/L	11.4%	15.4%	4.0%	7.5%	5.3%	9.0%
Ceftazidime > 1 mg/L	4.3%	3.8%	0.0%	0.0%	0.0%	2.0%
Either of above	12.9%	15.4%	4.0%	7.5%	5.3%	9.5%
Confirmed						
any ESBL (No. received)	2/6	1/4	0/1	1/3	0/2	4/16
CTX-M types	2	0	0	0	0	2
plasmid-borne AmpC	0	0	0	0	0	0
***Enterobacter* species**	24	13	10	21	3	71
Cefepime > 1 mg/L	10.6%	8.6%	13.0%	10.7%	3.0%	9.5%
Confirmed						
any ESBL (No. received)	9/22	6/12	3/9	6/18	1/3	25/64
CTX-M types	0	0	0	1	1	2

Based on the tests performed in this study, ESBLs appear most common in *Enterobacter* species. Thirty nine percent of *Enterobacter* spp. with cefepime MIC >1 mg/L referred for molecular characterisation were confirmed to contain ESBLs. ESBLs are more common in *Klebsiella* species than in *E. coli*, a situation that has prevailed in Australia since their original emergence here. ESBL-producing strains do not appear to be becoming more common in Australia, perhaps as a consequence of control policies for third-generation cephalosporin use. Over 93% of *E. coli* and *K. pneumoniae* with ceftriaxone or ceftazidime MIC >1 mg/L that were available for molecular characterization were confirmed to contain one or more ESBL genes. Five isolates of *E. coli* were examined using an allele-specific PCR for the *pabB* gene as a screen for isolates belonging to highly virulent O25b-ST131 clone. One O25b-ST131 *E. coli* was confirmed.

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

6.3.2 PLASMID-BORNE AmpC ß-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 uncommon species onto transmissible plasmids and into the common pathogens. Already there are 6 separate classes. Like ESBLs these enzymes confer resistance to the important third-generation cephalosporins. Routine 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 AmpC enzymes, namely their chromosomal cephalosporinases.

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

Species	NSW/ACT	QLD/NT	SA	VIC/TAS	WA	Australia
E. coli	6	4	4	3	3	20
Cefoxitin ≥ 32 mg/L	2.7%	2.7%	4.0%	1.6%	3.0%	2.6%
***Klebsiella* species**	13	4	2	2	0	21
Cefoxitin ≥ 32 mg/L	6.0%	2.7%	2.5%	1.2%	0.0%	2.9%

The proportions of *E. coli* and *Klebsiella* species with elevated cefoxitin MICs was low. Only 23% of cefoxitin-resistant *E. coli* and 9.1% of *Klebsiella* spp. that were available for molecular confirmation were confirmed to contain plasmid-borne AmpC; with CMY-2 (n=3) in *E. coli,* and DHA detected in one *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 for the first time among members of the Enterobacteriaceae. One strain of *Klebsiella pneumoniae* and four *Enterobacter* species were not susceptible to meropenem. The strains came from 5 institutions in 4 states. In one of these strains (*K. pneumoniae*), the presence of a carbapenemase was confirmed by molecular methods [bla_{IMP-4}]. These are among the first known incidences of metallo-ß-lactamases in Australia. These are particularly troublesome resistance mechanisms as they inactivate a broad range of ß-lactams including the last-line carbapenems. Recent experience in one institution has shown that this resistance mechanism can spread amongst a range of Gram-negatives. OXA-23 was found in all strains of *A. baumannii* that were available for molecular follow-up (n=28).

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), i.e. with presumptive extended-spectrum ß-lactamases, which were resistant to other drug classes is shown in Table 22:

Table 22. Co-resistance percentages in strains presumptively harbouring ESBLs

Species	Category	Ciprofloxacin	Gentamicin	Trimethoprim*
E. coli (n=23)	%I	0.0%	0.0%	-
	%R	43.5%	56.5%	73.9%
Klebsiella pneumoniae (n=21)	%I	4.8%	0.0%	-
	%R	28.6%	66.7%	57.1%
Enterobacter species (n=71)	%I	4.2%	1.4%	-
	%R	9.9%	28.2%	36.6%

* 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.

Some clustering of resistance was noticeable in *E. coli*, as acquired resistance to 6 agents was more common than acquired resistance to 5 agents. Although multi-drug resistance is common in *Acinetobacter* species, there is currently no consensus definition of how multidrug resistance should be defined. An indication of their frequency in this surveillance program can be ascertained from the Table in Appendix 2.

Table 23. Multi-resistance in Escherichia coli

		Non-multi-resistant					Multi-resistant										
Region	*Total*	*0*	*1*	*2*	*3*	*%*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*%*
NSW/ACT	223	98	64	24	20	92.4%	9	2	3	1	2							7.6%
QLD/NT	150	82	34	20	9	96.7%	3			1	1							3.3%
SA	99	53	23	13	2	91.9%	2	3	3									8.1%
VIC/TAS	190	84	54	30	11	94.2%	6	1	4									5.8%
WA	100	47	21	19	8	95.0%	3		1		1							5.0%
Australia	*762*	*364*	*196*	*106*	*50*	*94.0%*	*23*	6	*11*	2	4							*6.0%*

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

Antibiotics excluded: Cephalothin, 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*	*%*
NSW/ACT	215	133	51	6	9	92.6%	5	3	2	5	1			7.4%
QLD/NT	147	102	29	5	7	97.3%	1	1	1		1			2.7%
SA	79	40	31	4	1	96.2%	1	1		1				3.8%
VIC/TAS	173	88	71	6	2	96.5%	1	4				1		3.5%
WA	98	56	34	4	1	96.9%	3							3.1%
Australia	*712*	*419*	*216*	*25*	*20*	*95.5%*	*11*	*9*	*3*	*6*	*2*	*1*		*4.5%*

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

Antibiotics excluded: ampicillin, cephalothin, 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*	*%*
NSW/ACT	226	112	31	37	23	89.8%	17	5	1					10.2%
QLD/NT	151	93	24	14	11	94.0%	7	2						6.0%
SA	77	40	6	14	10	90.9%	3	3	1					9.1%
VIC/TAS	197	92	36	36	23	94.9%	5	4	1					5.1%
WA	99	67	14	13	4	99.0%	1							1.0%
Australia	*750*	*404*	*111*	*114*	*71*	*93.3%*	*33*	*14*	*3*					*6.7%*

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

Antibiotics excluded: ampicillin, amoxycillin-clavulanate, cephalothin, 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. As such simple denominators such as occupied bed days over the period of collection would not provide meaningful comparisons between institutions.

2. Apart from blood cultures and sterile site isolates, the clinical significance of the isolates cannot be ascertained with certainty. 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.

3. Laboratory to laboratory variation was noted with the tigecycline Etest, driven by individual laboratory choice of agar medium and brand. This made the detection of true resistance unreliable.

7 STANDARDS AND INFORMATION RESOURCES

1. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twentieth informational supplement. M100-S20. CLSI, Wayne, Pa, 2010.

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.

4. Tigecycline USA package insert; www.wyeth.com/hcp/tygacil/moa

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APPENDIX 1. SUSCEPTIBILITY RESULTS BY STATE AND SOURCE

Ampicillin

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	8.3%	25.0%	66.7%
		QLD/NT	11	9.1%	36.4%	54.5%
		SA	9	11.1%	55.6%	33.3%
		VIC/TAS	11		18.2%	81.8%
		WA	13	23.1%	23.1%	53.8%
		Total	*56*	*10.7%*	*30.4%*	*58.9%*
	Other	NSW/ACT	214	13.6%	26.6%	59.8%
		QLD/NT	140	12.9%	22.1%	65.0%
		SA	68	13.2%	26.5%	60.3%
		VIC/TAS	186	21.0%	17.2%	61.8%
		WA	86	23.3%	27.9%	48.8%
		Total	*694*	*16.6%*	*23.3%*	*60.1%*
		National	750	121	179	450
				16.1%	23.9%	60.0%
Escherichia coli	Blood	NSW/ACT	89	47.2%	2.2%	50.6%
		QLD/NT	56	46.4%	1.8%	51.8%
		SA	41	56.1%	4.9%	39.0%
		VIC/TAS	57	38.6%	1.8%	59.6%
		WA	19	52.6%	47.4%	
		Total	*262*	*46.9%*	*2.3%*	*50.8%*
	Other	NSW/ACT	134	47.0%		53.0%
		QLD/NT	94	60.6%	2.1%	37.2%
		SA	58	60.3%		39.7%
		VIC/TAS	133	50.4%	1.5%	48.1%
		WA	81	50.6%		49.4%
		Total	*500*	*52.6%*	*0.8%*	*46.6%*
		National	762	386	10	366
				50.7%	1.3%	48.0%
Klebsiella species	Blood	NSW/ACT	56	1.8%	33.9%	64.3%
		QLD/NT	40	2.5%	22.5%	75.0%
		SA	15		46.7%	53.3%
		VIC/TAS	42	2.4%	31.0%	66.7%
		WA	22		18.2%	81.8%
		Total	*175*	*1.7%*	*29.7%*	*68.6%*
	Other	NSW/ACT	159	1.9%	27.0%	71.1%
		QLD/NT	107	1.9%	24.3%	73.8%
		SA	64		14.1%	85.9%
		VIC/TAS	131	3.8%	27.5%	68.7%
		WA	76	7.9%	23.7%	68.4%
		Total	*537*	*3.0%*	*24.6%*	*72.4%*
		National	712	19	184	509
				2.7%	25.8%	71.5%

Amoxycillin-clavulanate

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	8.3%	9.8.3%	83.3%
		QLD/NT	11		9.1%	90.9%
		SA	9		33.3%	66.7%
		VIC/TAS	11	18.2%		81.8%
		WA	13	30.8%	7.7%	61.5%
		Total	*56*	*12.5%*	*10.7%*	*76.8%*
	Other	NSW/ACT	214	8.9%	5.6%	85.5%
		QLD/NT	140	10.7%	5.0%	84.3%
		SA	68	10.3%	4.4%	85.3%
		VIC/TAS	186	12.9%	4.8%	82.3%
		WA	86	15.1%	5.8%	79.1%
		Total	*694*	*11.2%*	*5.2%*	*83.6%*
		National	*750*	*85*	*42*	*623*
				11.3%	*5.6%*	*83.1%*
Escherichia coli	Blood	NSW/ACT	89	88.8%	9.0%	2.2%
		QLD/NT	56	76.8%	14.3%	8.9%
		SA	41	92.7%	7.3%	
		VIC/TAS	57	78.9%	14.0%	7.0%
		WA	19	84.2%	10.5%	5.3%
		Total	*262*	*84.4%*	*11.1%*	*4.6%*
	Other	NSW/ACT	134	79.9%	11.2%	9.0%
		QLD/NT	94	89.4%	9.6%	1.1%
		SA	58	86.2%	6.9%	6.9%
		VIC/TAS	133	80.5%	15.0%	4.5%
		WA	81	76.5%	16.0%	7.4%
		Total	*500*	*82.0%*	*12.2%*	*5.8%*
		National	762	631	90	41
				82.8%	11.8%	5.4%
Klebsiella species	Blood	NSW/ACT	56	94.6%		5.4%
		QLD/NT	40	92.5%	7.5%	
		SA	15	100%		
		VIC/TAS	42	92.9%	4.8%	2.4%
		WA	22	100%		
		Total	*175*	*94.9%*	*2.9%*	*2.3%*
	Other	NSW/ACT	159	93.1%	2.5%	4.4%
		QLD/NT	107	89.7%	7.5%	2.8%
		SA	64	95.3%	1.6%	3.1%
		VIC/TAS	131	94.7%	3.8%	1.5%
		WA	76	93.4%	2.6%	3.9%
		Total	*537*	*93.1%*	*3.7%*	*3.2%*
		National	712	666	25	21
				93.5%	3.5%	2.9%

Ticarcillin-clavulanate

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	75.0%		25.0%
		QLD/NT	11	100%		
		SA	9	77.8%		22.2%
		VIC/TAS	11	54.5%	18.2%	27.3%
		WA	13	76.9%	15.4%	7.7%
		Total	*56*	*76.8%*	*7.1%*	*16.1%*
	Other	NSW/ACT	214	65.4%	3.7%	30.8%
		QLD/NT	140	76.4%	5.0%	18.6%
		SA	68	63.2%	7.4%	29.4%
		VIC/TAS	186	61.3%	9.7%	29.0%
		WA	86	80.2%	4.7%	15.1%
		Total	*694*	*68.2%*	*6.1%*	*25.8%*
		National	750	516	46	188
				68.8%	6.1%	25.1%
Escherichia coli	Blood	NSW/ACT	89	91.0%	5.6%	3.4%
		QLD/NT	56	85.7%	7.1%	7.1%
		SA	41	92.7%	7.3%	
		VIC/TAS	57	84.2%	8.8%	7.0%
		WA	19	89.5%	10.5%	
		Total	*262*	*88.5%*	*7.3%*	*4.2%*
	Other	NSW/ACT	134	88.1%	9.7%	2.2%
		QLD/NT	94	91.5%	3.2%	5.3%
		SA	58	87.9%	6.9%	5.2%
		VIC/TAS	133	86.5%	11.3%	2.3%
		WA	81	85.2%	8.6%	6.2%
		Total	*500*	*87.8%*	*8.4%*	*3.8%*
		National	762	671	61	30
				88.1%	8.0%	3.9%
Klebsiella species	Blood	NSW/ACT	56	94.6%	3.6%	1.8%
		QLD/NT	40	92.5%	5.0%	2.5%
		SA	15	100%		
		VIC/TAS	42	95.2%		4.8%
		WA	22	100%		
		Total	*175*	*95.4%*	*2.3%*	*2.3%*
	Other	NSW/ACT	159	90.6%	3.1%	6.3%
		QLD/NT	107	91.6%	4.7%	3.7%
		SA	64	95.3%	3.1%	1.6%
		VIC/TAS	131	96.2%	1.5%	2.3%
		WA	76	93.4%	1.3%	5.3%
		Total	*537*	*93.1%*	*2.8%*	*4.1%*
		National	712	667	19	26

Piperacillin-tazobactam

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	91.7%	8.3%	
		QLD/NT	11	100%		
		SA	9	88.9%		11.1%
		VIC/TAS	11	72.7%	27.3%	
		WA	13	100%		
		Total	*56*	*91.1%*	*7.1%*	*1.8%*
	Other	NSW/ACT	214	74.8%	22.0%	3.3%
		QLD/NT	140	82.9%	10.0%	7.1%
		SA	68	70.6%	23.5%	5.9%
		VIC/TAS	186	73.7%	19.4%	7.0%
		WA	86	91.9%	7.0%	1.2%
		Total	*694*	*77.8%*	*17.1%*	*5.0%*
		National	750	591	123	36
				78.8%	16.4%	4.8%
Escherichia coli	Blood	NSW/ACT	89	98.9%	1.1%	
		QLD/NT	56	100%		
		SA	41	100%		
		VIC/TAS	57	96.5%	3.5%	
		WA	19	100%		
		Total	*262*	*98.9%*	*1.1%*	
	Other	NSW/ACT	134	100%		
		QLD/NT	94	97.9%	1.1%	1.1%
		SA	58	100%		
		VIC/TAS	133	100%		
		WA	81	97.5%		2.5%
		Total	*500*	*99.2%*	*0.2%*	*0.6%*
		National	762	755	4	3
				99.1%	0.5%	0.4%
Klebsiella species	Blood	NSW/ACT	56	98.2%		1.8%
		QLD/NT	40	95.0%		5.0%
		SA	15	93.3%	6.7%	
		VIC/TAS	42	97.6%		2.4%
		WA	22	100%		
		Total	*175*	*97.1%*	*0.6%*	*2.3%*
	Other	NSW/ACT	159	94.3%	1.9%	3.8%
		QLD/NT	107	95.3%	1.9%	2.8%
		SA	64	96.9%	1.6%	1.6%
		VIC/TAS	131	97.7%	1.5%	0.8%
		WA	76	97.4%		2.6%
		Total	*537*	*96.1%*	*1.5%*	*2.4%*
		National	712	686	9	17
				96.3%	1.3%	2.4%

Cephalothin

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12			100%
		QLD/NT	11			100%
		SA	9		22.2%	77.8%
		VIC/TAS	11			100%
		WA	13	7.7%	7.7%	84.6%
		Total	*56*	*1.8%*	*5.4%*	*92.9%*
	Other	NSW/ACT	214	3.3%	11.7%	85.0%
		QLD/NT	140	1.4%	7.1%	91.4%
		SA	68	4.4%	2.9%	92.6%
		VIC/TAS	186	4.8%	6.5%	88.7%
		WA	86	1.2%	11.6%	87.2%
		Total	*694*	*3.2%*	*8.5%*	*88.3%*
		National	750	23	62	665
				3.1%	8.3%	88.7%
Escherichia coli	Blood	NSW/ACT	89	60.7%	31.5%	7.9%
		QLD/NT	56	58.9%	26.8%	14.3%
		SA	41	65.9%	19.5%	14.6%
		VIC/TAS	57	57.9%	22.8%	19.3%
		WA	19	73.7%	21.1%	5.3%
		Total	*262*	*61.5%*	*26.0%*	*12.6%*
	Other	NSW/ACT	134	48.5%	36.6%	14.9%
		QLD/NT	94	61.7%	28.7%	9.6%
		SA	58	67.2%	15.5%	17.2%
		VIC/TAS	133	57.1%	28.6%	14.3%
		WA	81	49.4%	33.3%	17.3%
		Total	*500*	*55.6%*	*30.0%*	*14.4%*
		National	762	439	218	105
				57.6%	28.6%	13.8%
Klebsiella species	Blood	NSW/ACT	56	87.5%	3.6%	18.9%
		QLD/NT	40	85.0%	5.0%	10.0%
		SA	15	86.7%		13.3%
		VIC/TAS	42	90.5%	2.4%	7.1%
		WA	22	100%		
		Total	*175*	*89.1%*	*2.9%*	*8.0%*
	Other	NSW/ACT	159	84.3%	3.8%	11.9%
		QLD/NT	107	88.8%	2.8%	8.4%
		SA	64	92.2%	1.6%	6.3%
		VIC/TAS	131	87.8%	3.8%	8.4%
		WA	76	92.1%	1.3%	6.6%
		Total	*537*	*88.1%*	*3.0%*	*8.9%*
		National	712	629	21	62
				88.3%	2.9%	8.7%

Cefazolin

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	8.3%		91.7%
		QLD/NT	11			100%
		SA	9			100%
		VIC/TAS	11			100%
		WA	13	15.4%		84.6%
		Total	*56*	*5.4%*		*94.6%*
	Other	NSW/ACT	214	7.5%		92.5%
		QLD/NT	140	5.7%		94.3%
		SA	68	2.9%		97.1%
		VIC/TAS	186	6.5%		93.5%
		WA	86	4.7%		95.3%
		Total	*694*	*6.1%*		*93.9%*
		National	750	45		705
				6.0%		94.0%
Escherichia coli	Blood	NSW/ACT	89	89.9%		10.1%
		QLD/NT	56	87.5%		12.5%
		SA	41	90.2%		9.8%
		VIC/TAS	57	82.5%		17.5%
		WA	19	89.5%		10.5%
		Total	*262*	*87.8%*		*12.2%*
	Other	NSW/ACT	134	84.3%		15.7%
		QLD/NT	94	88.3%		11.7%
		SA	58	79.3%		20.7%
		VIC/TAS	133	87.2%		12.8%
		WA	81	77.8%		22.2%
		Total	*500*	*84.2%*		*15.8%*
		National	762	651		111
				85.4%		14.6%
Klebsiella species	Blood	NSW/ACT	56	85.7%		14.3%
		QLD/NT	40	77.5%		22.5%
		SA	15	86.7%		13.3%
		VIC/TAS	42	88.1%		11.9%
		WA	22	81.8%		18.2%
		Total	*175*	*84.0*		*16.0%*
	Other	NSW/ACT	159	73.6%		26.4%
		QLD/NT	107	84.1%		15.9%
		SA	64	75.0%		25.0%
		VIC/TAS	131	75.6%		24.4%
		WA	76	69.7%		30.3%
		Total	*537*	*75.8%*		*24.2%*
		National	712	554		158
				77.8%		22.2%

Ceftriaxone

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	75.0%		25.0%
		QLD/NT	11	90.9%	9.1%	
		SA	9	100%		
		VIC/TAS	11	63.6%		36.4%
		WA	13	84.6%		15.4%
		Total	*56*	*82.1%*	*1.8%*	*16.1%*
	Other	NSW/ACT	214	63.6%	1.4%	3435.0%
		QLD/NT	140	74.3%	0.7%	25.0%
		SA	68	61.8%	1.5%	36.8%
		VIC/TAS	186	61.3%	1.1%	37.6%
		WA	86	79.1%	1.2%	19.8%
		Total	*694*	*66.9%*	*1.2%*	*332.0%*
		National	750	510	9	232
				68.0%	1.2%	30.8%
Escherichia coli	Blood	NSW/ACT	89	98.9%		1.1%
		QLD/NT	56	98.2%		1.8%
		SA	41	100%		
		VIC/TAS	57	96.5%		3.5%
		WA	19	100%		
		Total	*262*	*98.5%*		*1.5%*
	Other	NSW/ACT	134	94.8%		5.2%
		QLD/NT	94	98.9%		1.1%
		SA	58	93.1%		6.9%
		VIC/TAS	133	98.5%		1.5%
		WA	81	97.5%		2.5%
		Total	*500*	*96.8%*		*3.2%*
		National	762	742		20
				97.4%		2.6%
Klebsiella species	Blood	NSW/ACT	56	96.4%		3.6%
		QLD/NT	40	92.5%		7.5%
		SA	15	93.3%		6.7%
		VIC/TAS	42	95.2%		4.8%
		WA	22	100%		
		Total	*175*	*95.4%*		*4.6%*
	Other	NSW/ACT	159	90.6%	0.6%	8.8%
		QLD/NT	107	95.3%	0.9%	3.7%
		SA	64	96.9%		3.1%
		VIC/TAS	131	94.7%	0.8%	4.6%
		WA	76	96.1%		3.9%
		Total	*537*	*94.0%*	*0.6%*	*5.4%*
		National	712	672	3	37
				94.4%	0.4%	5.2%

Ceftazidime

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	75.0%		25.0%
		QLD/NT	11	90.9%		9.1%
		SA	9	88.9%		11.1%
		VIC/TAS	11	63.6%		36.4%
		WA	13	92.3%		7.7%
		Total	*56*	*82.1%*		*17.9%*
	Other	NSW/ACT	214	64.5%	0.5%	35.0%
		QLD/NT	140	77.1%		22.9%
		SA	68	64.7%		35.3%
		VIC/TAS	186	66.1%	1.1%	32.8%
		WA	86	83.7%	2.3%	14.0%
		Total	*694*	*69.9%*	*0.7%*	*29.4%*
		National	750	531	5	214
				70.8%	0.7%	28.5%
Escherichia coli	Blood	NSW/ACT	89	100%		
		QLD/NT	56	98.2%		1.8%
		SA	41	100%		
		VIC/TAS	57	96.5%		3.5%
		WA	19	100%		
		Total	*262*	*98.9%*		*1.1%*
	Other	NSW/ACT	134	96.3%	0.7%	3.0%
		QLD/NT	94	100%		
		SA	58	100%		
		VIC/TAS	133	99.2%	0.8%	
		WA	81	97.5%	2.5%	
		Total	*500*	*98.4%*	*0.2%*	*1.4%*
		National	762	751	1	10
				98.6%	0.1%	1.3%
Klebsiella species	Blood	NSW/ACT	56	96.4%		3.6%
		QLD/NT	40	100%		
		SA	15	93.3%		6.7%
		VIC/TAS	42	97.6%		2.4%
		WA	22	100%		
		Total	*175*	*97.7%*		*2.3%*
	Other	NSW/ACT	159	95.0%		5.0%
		QLD/NT	107	99.1%		0.9%
		SA	64	98.4%		1.6%
		VIC/TAS	131	97.7%		2.3%
		WA	76	98.7%		1.3%
		Total	*537*	*97.4%*		*2.6%*
		National	712	694		18
				97.5%		2.5%

Cefepime

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	100%		
		QLD/NT	11	100%		
		SA	9	88.9%		11.1%
		VIC/TAS	11	100%		
		WA	13	100%		
		Total	*56*	*98.2%*		*1.8%*
	Other	NSW/ACT	214	100%		
		QLD/NT	140	100%		
		SA	68	97.1%		2.9%
		VIC/TAS	186	98.9%	0.5%	0.5%
		WA	86	100%		
		Total	*694*	*99.4%*	*0.1%*	*0.4%*
		National	750	745	1	4
				99.3%	0.1%	0.5%
Escherichia coli	Blood	NSW/ACT	89	100%		
		QLD/NT	56	100%		
		SA	41	100%		
		VIC/TAS	57	100%		
		WA	19	100%		
		Total	*262*	*100%*		
	Other	NSW/ACT	134	100%		
		QLD/NT	94	100%		
		SA	58	100%		
		VIC/TAS	133	100%		
		WA	81	100%		
		Total	*500*	*100%*		
		National	762	762		
				100%		
Klebsiella species	Blood	NSW/ACT	56	96.4%		3.6%
		QLD/NT	40	100%		
		SA	15	100%		
		VIC/TAS	42	100%		
		WA	22	100%		
		Total	*175*	*98.9%*		*1.1%*
	Other	NSW/ACT	159	98.1%		1.9%
		QLD/NT	107	100%		
		SA	64	100%		
		VIC/TAS	131	98.5%		1.5%
		WA	76	100%		
		Total	*537*	*99.1%*		*0.9%*
		National	712	705		7
				99.0%		1.0%

Meropenem

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	100%		
		QLD/NT	11	100%		
		SA	9	88.9%		11.1%
		VIC/TAS	11	100%		
		WA	13	100%		
		Total	*56*	*98.2%*		*1.8%*
	Other	NSW/ACT	214	99.5%		0.5%
		QLD/NT	140	99.3%		0.7%
		SA	68	98.5%		1.5%
		VIC/TAS	186	100%		
		WA	86	100%		
		Total	*694*	*99.6%*		*0.4%*
		National	750	746		4
				99.5%		0.5%
Escherichia coli	Blood	NSW/ACT	89	100%		
		QLD/NT	56	100%		
		SA	41	100%		
		VIC/TAS	57	100%		
		WA	19	100%		
		Total	*262*	*100%*		
	Other	NSW/ACT	134	100%		
		QLD/NT	94	100%		
		SA	58	100%		
		VIC/TAS	133	100%		
		WA	81	100%		
		Total	*500*	*100%*		
		National	762	762		
				100%		
Klebsiella species	Blood	NSW/ACT	56	100%		
		QLD/NT	40	100%		
		SA	15	100%		
		VIC/TAS	42	100%		
		WA	22	100%		
		Total	*175*	*100%*		
	Other	NSW/ACT	160	100%		
		QLD/NT	107	100%		
		SA	64	100%		
		VIC/TAS	131	99.2%	0.8%	
		WA	76	100%		
		Total	*537*	*99.8%*	*0.2%*	
		National	712	711	1	
				99.9%	0.1%	

Ciprofloxacin

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	100%		
		QLD/NT	11	100%		
		SA	9	100%		
		VIC/TAS	11	100%		
		WA	13	100%		
		Total	*56*	*100%*		
	Other	NSW/ACT	214	94.4%	2.3%	3.3%
		QLD/NT	140	98.6%	0.7%	0.7%
		SA	68	95.6%		4.4%
		VIC/TAS	186	97.3%		2.7%
		WA	86	96.5%		3.5%
		Total	*694*	*96.4%*	*0.9%*	*2.7%*
		National	750	725	6	19
				96.7%	0.8%	2.5%
Escherichia coli	Blood	NSW/ACT	89	92.1%	1.1%	6.7%
		QLD/NT	56	98.2%		1.8%
		SA	41	95.1%		4.9%
		VIC/TAS	57	96.5%		3.5%
		WA	19	94.7%		5.3%
		Total	*262*	*95.0%*	*0.4%*	*4.6%*
	Other	NSW/ACT	134	94.0%		6.0%
		QLD/NT	94	97.9%		2.1%
		SA	58	93.1%		6.9%
		VIC/TAS	133	94.7%		5.3%
		WA	81	96.3%		3.7%
		Total	*500*	*95.2%*		*4.8%*
		National	762	725	1	36
				95.1%	0.1%	4.7%
Klebsiella species	Blood	NSW/ACT	56	96.4%		3.6%
		QLD/NT	40	95.0%		5.0%
		SA	15	93.3%		6.7%
		VIC/TAS	42	100%		
		WA	22	100%		
		Total	*175*	*97.1%*		*2.9%*
	Other	NSW/ACT	159	96.2%	0.6%	3.1%
		QLD/NT	107	97.2%	1.9%	0.9%
		SA	64	98.4%		1.6%
		VIC/TAS	131	98.5%		1.5%
		WA	76	98.7%		1.3%
		Total	*537*	*97.6%*	*0.6%*	*1.9%*
		National	712	694	3	15
				97.5%	0.4%	2.1%

Gentamicin

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	83.3%		16.7%
		QLD/NT	11	90.9%		9.1%
		SA	9	100%		
		VIC/TAS	11	100%		
		WA	13	100%		
		Total	*56*	*94.6%*		*5.4%*
	Other	NSW/ACT	214	87.9%	0.9%	11.2%
		QLD/NT	140	92.9%	0.7%	6.4%
		SA	68	89.7%	1.5%	8.8%
		VIC/TAS	186	95.7%	1.6%	2.7%
		WA	86	100%		
		Total	*694*	*92.7%*	*1.0%*	*6.3%*
		National	750	696	7	47
				92.8%	0.9%	6.3%
Escherichia coli	Blood	NSW/ACT	89	92.1%	1.1%	6.7%
		QLD/NT	56	96.4%		3.6%
		SA	41	95.1%		4.9%
		VIC/TAS	57	94.7%		5.3%
		WA	19	94.7%		5.3%
		Total	*262*	*94.3%*	*0.4%*	*5.3%*
	Other	NSW/ACT	134	93.3%		6.7%
		QLD/NT	94	97.9%	1.1%	1.1%
		SA	58	91.4%		8.6%
		VIC/TAS	133	96.2%		3.8%
		WA	81	100%		
		Total	*500*	*95.8%*	*0.2%*	*4.0%*
		National	762	726	2	34
				95.3%	0.3%	4.5%
Klebsiella species	Blood	NSW/ACT	56	96.4%		3.6%
		QLD/NT	40	95.0%		5.0%
		SA	15	100%		
		VIC/TAS	42	97.6%		2.4%
		WA	22	100%		
		Total	*175*	*97.1%*		*2.9%*
	Other	NSW/ACT	159	96.2%		3.8%
		QLD/NT	107	97.2%		2.8%
		SA	64	98.4%		1.6%
		VIC/TAS	131	96.9%		3.1%
		WA	76	98.7%		1.3%
		Total	*537*	*97.2%*		*2.8%*
		National	712	692		20
				97.2%		2.8%

Trimethoprim

Genus	Source	Region	Total	%S	%I	%R
Enterobacter species	Blood	NSW/ACT	12	75.0%		25.0%
		QLD/NT	11	81.8%		18.2%
		SA	9	88.9%		11.1%
		VIC/TAS	11	90.9%		9.1%
		WA	13	100%		
		Total	*56*	*87.5%*		*12.5%*
	Other	NSW/ACT	214	83.2%		16.8%
		QLD/NT	140	87.9%		12.1%
		SA	68	80.9%		19.1%
		VIC/TAS	186	89.8%		10.2%
		WA	86	97.7%		2.3%
		Total	*694*	*87.5%*		*12.5%*
		National	750	656		94
				87.5%		12.5%
Escherichia coli	Blood	NSW/ACT	89	71.9%		28.1%
		QLD/NT	56	78.6%		21.4%
		SA	41	82.9%		17.1%
		VIC/TAS	57	77.2%		22.8%
		WA	19	89.5%		10.5%
		Total	*262*	*77.5%*		*22.5%*
	Other	NSW/ACT	134	80.6%		19.4%
		QLD/NT	94	86.2%		13.8%
		SA	58	84.5%		15.5%
		VIC/TAS	133	81.2%		18.8%
		WA	81	79.0%		21.0%
		Total	*500*	*82.0%*		*18.0%*
		National	762	613		149
				80.4%		19.6%
Klebsiella species	Blood	NSW/ACT	56	92.9%		7.1%
		QLD/NT	40	95.0%		5.0%
		SA	15	93.3%		6.7%
		VIC/TAS	42	97.6%		2.4%
		WA	22	100%		
		Total	*175*	*95.4%*		*4.6%*
	Other	NSW/ACT	159	92.5%		7.5%
		QLD/NT	107	87.9%		12.1%
		SA	64	87.5%		12.5%
		VIC/TAS	131	94.7%		5.3%
		WA	76	97.4%		2.6%
		Total	*537*	*92.2%*		*7.8%*
		National	712	662		50
				93.0%		7.0%

APPENDIX 2. ANTIBIOTIC PROFILES BY FREQUENCY

***Enterobacter* species** (n = 750)

PtzCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/ACT	VIC/TAS	SA	WA
Nit	349	84	87	91	32	55
	120	18	44	23	13	22
PtzCtrCaz Nit	85	6	30	32	11	6
PtzCtrCaz	37	11	10	11	4	1
TmpNit	19	8	6	4	1	
CtrCaz Nit	19	3	4	6		6
Ctr Nit	12	3	1	4		4
CtrCaz Gen TmpNit	11	2	5	2	2	
CtrCaz Gen Tmp	9	3	3	1	2	
Tmp	6	1	3	1	1	
Ctr	6	1	1	4		
PtzCtrCaz TmpNit	6	1	1	2	2	
PtzCtrCaz Gen Tmp	5		5			
CtrCaz	5		3	1	1	
CtrCaz TmpNit	4		2	2		
PtzCtrCaz Tmp	4	2	2			
PtzCtrCaz Gen TmpNit	4		1	3		
PtzCtrCaz Gen TmpNitCip	4		4			
TmpNitCip	3		1	1	1	
NitCip	2					2
Ctr TmpNit	2			1	1	
CtrCaz Tmp	2			1		1
CtrCaz Gen	2	1	1			
CtrCaz Gen Nit	2		1	1		
CtrCaz Gen Tmp Cip	2	1	1			
PtzCtrCaz NitCip	2			2		
PtzCtrCaz Gen Nit	2	2				
Tmp Cip	1				1	
Gen	1		1			
Gen NitCip	1		1			
Gen Tmp	1		1			
Gen TmpNitCip	1	1				
Caz Nit	1			1		
Caz Gen TmpNitCip	1		1			
Ctr Cip	1		1			
Ctr Tmp	1					1
Ctr Gen Nit	1	1				
Ctr Gen Tmp	1				1	
Ctr Gen TmpNitCip	1			1		
CtrCaz NitCip	1					1
CtrCaz TmpNitCip	1		1			
CtrCaz Gen -	1		1			
CtrCaz Gen Mer	1		1			
Ptz Nit	1	1				
Ptz TmpNitCip	1				1	
Ptz Caz Nit Mer	1	1				

PtzCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/ACT	VIC/TAS	SA	WA
Ptz CazCpm Nit Mer	1				1	
PtzCtrCaz Tmp Cip	1		1			
PtzCtrCaz Gen Tmp Cip	1		1			
PtzCtrCazCpm Nit	1			1		
PtzCtrCazCpm TmpNitCip	1			1		
PtzCtrCazCpmGen TmpNit	1				1	
PtzCtrCazCpmGenAmk Nit Mer	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 = 762)

AmpAmcPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/ACT	VIC/TAS	SA	WA
	349	77	96	81	50	45
Amp	141	27	47	39	15	13
Amp Tmp	48	11	13	13	4	7
AmpAmc	35	6	12	11	2	4
AmpAmc Czl	28	2	3	9	5	9
Tmp	26	3	9	5	5	4
AmpAmc Czl Tmp	21	4	7	6	1	3
AmpAmc CzlCft	12	2	6	1	1	2
Amp Czl	11	2	1	3	3	2
Amp Gen Tmp Cip	6		2	2	1	1
Amp Gen Tmp	5	1	3	1		
AmpAmc Tmp	5		3	2		
Nit	4			1	3	
Amp Tmp Cip	4		4			
Cip	3	1		2		
Cft	3	1				2
Amp Cip	3		1	1		1
Amp Nit	3	1		1		1
Amp Czl Tmp	3	1		1		1
Amp Czl Ctr Gen Tmp Cip	3		2		1	
AmpAmcPtzCzl	3	1	1			1
Amp Gen	2		1		1	
Amp Cft	2	1			1	
Amp Czl Ctr Gen Tmp	2		1		1	
AmpAmc CzlCftCtrCaz	2			1		1
AmpAmc CzlCftCtrCaz Gen Tmp Cip	2		2			
AmpAmcPtzCzl Tmp	2	1		1		
Amc	1	1				
Amp TmpNit	1			1		
Amp Gen Cip	1		1			
Amp GenAmkTmp	1	1				
Amp Cft Cip	1				1	
Amp Cft Tmp Cip	1					1
Amp Cft Gen Tmp Cip	1		1			
Amp Czl TmpNit	1		1			
Amp Czl Gen	1			1		
Amp Czl Gen Tmp	1		1			
Amp Czl Gen TmpNitCip	1				1	
Amp Czl Ctr Gen TmpNitCip	1				1	
Amp Czl CtrCaz	1		1			
Amp CzlCft Gen Tmp	1		1			
AmpAmc Nit	1	1				
AmpAmc Gen Tmp	1			1		
AmpAmc Cft	1			1		
AmpAmc Cft Tmp Cip	1					1
AmpAmc Cft Gen Tmp Cip	1			1		
AmpAmc Czl Nit	1	1				

Amp	Amc	Ptz	Czl	Cft	Ctr	Caz	Cpm	Gen	Amk	Tmp	Nit	Cip	Mer	AUS	QLD/NT	NSW/ACT	VIC/TAS	SA	WA
Amp	Amc		Czl							Tmp		Cip		1	1				
Amp	Amc		Czl		Ctr					Tmp		Cip		1			1		
Amp	Amc		Czl		Ctr	Caz		Gen	Amk	Tmp				1			1		
Amp	Amc		Czl	Cft								Cip		1	1				
Amp	Amc		Czl	Cft							Nit			1		1			
Amp	Amc		Czl	Cft				Gen				Cip		1				1	
Amp	Amc		Czl	Cft				Gen		Tmp		Cip		1			1		
Amp	Amc		Czl	Cft	Ctr					Tmp				1				1	
Amp	Amc		Czl	Cft	Ctr			Gen		Tmp				1	1				
Amp	Amc		Czl	Cft	Ctr	Caz				Tmp		Cip		1		1			
Amp	Amc		Czl	Cft	Ctr	Caz		Gen				Cip		1		1			
Amp	Amc		Czl	Cft	Ctr	Caz		Gen		Tmp				1	1				
Amp	Amc	Ptz	Czl	Cft	Ctr	Caz				Tmp				1					1
Amp	Amc	Ptz	Czl	Cft	Ctr	Caz				Tmp		Cip		1			1		

Amp = ampicillin, Amc = amoxycillin-calvulanate, 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 = 712)

AmpPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/ACT	VIC/TAS	SA	WA
Nit	313	71	82	86	39	35
	196	34	71	42	15	34
Czl	82	12	22	19	12	17
TmpNit	16	6	3	4	2	1
Czl Nit	15	2	4	5	1	3
AmcPtzCzl Ctr	9	3	3	1	1	1
Tmp	6	2	1		3	
Cft Nit	6	1	2	2		1
Amc CzlCft Nit	5	2	3			
AmcPtzCzl Ctr Nit	4		2	1		1
TmpNitCip	3	1	1		1	
Czl Tmp	3		1	1	1	
Amc Nit	3	2		1		
Amc Czl	3			2		1
Cft	2		2			
Czl Ctr TmpNit	2		1	1		
Czl Ctr Gen Nit	2	1		1		
AmcPtzCzl Nit	2			1	1	
NitCip	1	1				
Gen Nit	1			1		
Cft NitCip	1		1			
Cft TmpNitCip	1		1			
Czl NitCip	1					1
Czl Gen NitCip	1		1			
Czl Caz TmpNit	1		1			
Czl Ctr Gen NitCip	1			1		
Czl Ctr Gen Tmp	1	1				
Czl CtrCaz TmpNit	1				1	
Czl CtrCaz Gen Nit	1					1
Czl CtrCaz Gen Tmp	1		1			
Czl CtrCazCpm TmpNitCip	1		1			
Czl CtrCazCpmGen TmpNit	1		1			
CzlCftCtr Gen TmpNitCip	1	1				
CzlCftCtrCazCpmGen Nit	1		1			
CzlCftCtrCazCpmGen TmpNit	1		1			
Ptz Cft NitCip	1				1	
PtzCzlCftCtrCaz AmkTmpNit	1		1			
PtzCzlCftCtrCaz Gen TmpNitCip	1		1			
Amc	1	1				
Amc Tmp	1	1				
Amc Czl Nit	1					1
Amc Czl TmpNit	1					1
Amc Czl Ctr Gen TmpNitCip	1	1				
Amc Czl Ctr CpmGen NitCip	1		1			
Amc Czl CtrCaz Amk Nit	1			1		
Amc Czl CtrCaz Gen Tmp	1			1		
Amc Czl CtrCazCpm Nit	1			1		

AmpPtzCzlCftCtrCazCpmGenAmkTmpNitCipMer	AUS	QLD/NT	NSW/ACT	VIC/TAS	SA	WA
Amc CzlCftCtrCaz	1		1			
Amc CzlCftCtrCaz Gen Nit	1		1			
Amc CzlCftCtrCaz Gen TmpNit	1				1	
AmcPtz TmpNit	1		1			
AmcPtz Cft Nit	1	1				
AmcPtzCzl	1	1				
AmcPtzCzl TmpNit	1	1				
AmcPtzCzlCft NitCip	1		1			
AmcPtzCzlCftCtr Nit	1		1			
AmcPtzCzlCftCtrCaz Gen TmpNitCip	1	1				
AmcPtzCzlCftCtrCazCpmGen Tmp CipMer	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

Acinetobacter species (n = 334)

PtzCtrCazCpmGenAmkSXTCipMer	AUS	QLD/NT	NSW/ACT	VIC/TAS	SA	WA
Ctr	106	28	26	21	16	15
	69	23	13	13	5	15
PtzCtrCazCpmGen SXTCipMer	51	23	25	3		
CtrCaz	35	14	3	4	7	7
PtzCtrCazCpm SXTCipMer	15	4	11			
CtrCazCpm	8	2	3	2		1
Ctr SXT	6	2	2	2		
CtrCazCpmGen SXTCip	6	1	1		4	
Ctr Gen Cip	4		4			
PtzCtrCazCpmGen SXTCip	4		2		2	
Ctr Cip	3			2		1
Ctr Gen SXTCip	3	1			1	1
CtrCazCpmGen Cip	3	1		2		
Gen Cip	2		2			
Ctr Gen SXT	2		2			
Ctr Cpm	2			1	1	
CtrCazCpm Cip	2		1			1
CtrCazCpm SXTCip	2		1		1	
CpmGen SXT	1	1				
CazCpmGen Cip	1			1		
Ctr Gen	1	1				
Ctr CpmGen SXTCip	1	1				
CtrCaz Cip	1		1			
CtrCaz SXT	1	1				
CtrCaz Gen SXT	1					1
CtrCazCpmGenAmkSXTCip	1			1		
PtzCtrCazCpm SXTCip	1	1				
PtzCtrCazCpm AmkSXTCipMer	1		1			
PtzCtrCazCpmGen CipMer	1		1			

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