NZ NAC New Zealand National Antimicrobial Susceptibility Testing Committee

NZ NAC CPE isolate survey - July 2019

In August 2018, the NZ NAC introduced guidelines for the 'minimum laboratory requirements for the detection of carbapenemase-producing Enterobacteriaceae from clinical samples and screening specimens'

As part of an annual review process to identify any shortfalls in the document, and to assess compliance to the standards, 3 isolates and a questionnaire were sent to each laboratory in June 2019. All results were received by 31st July.

The NZ NAC appreciates the time taken to undertake this testing and to complete the questionnaire. Overall laboratories performed very well, with most being able to comply with the minimum standards guidelines, identifying the presence or possibility of a carbapenemase in each isolate.

A few laboratories had trouble with NAC06, an OXA-48-producing *E. coli*. Oxacillinases are weak hydrolysers of carbapenems, making them a challenge to detect in a routine setting, particularly if there are no associated patient risk factors such as recent overseas travel/hospitalisation (NAC06 was isolated from a patient with a community-acquired infection and no overseas travel).

In order to increase the sensitivity of detection of these enzymes, laboratories should consider incorporating temocillin (either by disc or MIC methods) into their routine screening for resistance mechanisms, particularly when testing E. coli, K. oxytoca, K. pneumoniae and C. koseri.

Below is a summary of the findings from 21 participating laboratories. The expected results are on page 3.

Summary of methods and results

AMRS media

The most commonly used media type was FRL ESBLChrom, usually in conjunction with MacConkey Agar + 10 µg meropenem disc (the MacConkey plate gives an advantage of checking the integrity of the sample and for early detection of coliforms with a reduced zone to meropenem).

Other specialised screening media used by a few laboratories include Brilliance ESBL, CARBA SMART, CHROMagarKPC and mSUPERCARBA. Some laboratories do not routinely perform screening, so most incorporated AZT with routine blood agar plates.

Identification

NAC05: *Citrobacter freundii* complex	19/21 labs correct result
NAC06: *E. coli*	21/21 labs correct result
NAC07: *K. pneumoniae*	20/21 labs correct result

Carbapenemase production

NAC05 (**NDM-1**, CTX-M ESBL): 19/21 labs classified this isolate as a definite or probable carbapenemase producer. 7 laboratories were able to classify to NDM-type enzyme; with one laboratory adding the extra information of CTX-M Group 1 (includes CTX-M-15). Two laboratories were not sure, but said they would refer the isolate for further testing.

NAC06 (**OXA-48**, CTX-M ESBL): 18/21 labs classified this isolate as a definite or probable carbapenemase producer. 7 laboratories were able to classify to OXA-48-like enzyme; with one laboratory adding the extra information of CTX-M Group 9 (includes CTX-M-14). Three laboratories were unable to identify a carbapenemase, but picked up the ESBL.

NAC07 (**KPC-2**, CTX-M ESBL): 20/21 labs classified this isolate as a definite or probable carbapenemase producer. 7 laboratories were able to classify to KPC-type enzyme; with one laboratory adding the extra information of CTX-M Group 1. One laboratory reported an equivocal result, but said they would refer the isolate for further testing.

Carbapenemase detection methods

Screening

All laboratories used meropenem as part of their screening for carbapenemase producers, and all but 2 laboratories included piperacillin/tazobactam (tapi) as part of the screen. The combination of mero/tapi is recommended by EUCAST. Interestingly, meropenem testing by disc diffusion was superior to automated methods for screening purposes. 17/21 laboratories also included ertapenem – which is a sensitive marker for CPE, but not specific, especially in organisms that have intrinsic *ampC*. However ertapenem can be very useful for *E. coli* screening as it will detect possible OXA-48-producers. A number of laboratories also included temocillin as part of their ESBL/CPE work-up (either incorporated into Phoenix panels, or part of the ROSCO tablets or as separate disc testing).

Temocillin is particularly helpful for the detection of OXA-48-producers.

SCREENING Antibiotics	MIC	DISC
Mero (+erta clinical)		1
Mero /cefpodoxime		1
Mero/Tapi/cefpod		2
Mero/Tapi/Erta	1	1
Mero/Tapi (*erta disc)	3*	6
Mero/Tapi/Erta/Imip	5	1

Confirmation

Seven laboratories used molecular methods, including 4 labs using GeneXpert, and one of each lab using AusDiagnostics, BD-Max or Biotech NG Carba5. Of the phenotypic methods used, the mCIM test was a popular choice, with 11 laboratories using this simple and inexpensive method. 5 laboratories use the BD-Phoenix system which has CPO-detect incorporated into AST panels – this addition can be very handy, (although CPO-detect was falsely negative for NAC06). Other methods include in-house Carba NP or Rapidec Carba NP, ROSCO tablets, and one laboratory using MAST discs. Several labs had no confirmation tests, but would refer isolates to their referral lab or ESR. Of course, all CPE must be sent to ESR for reference/surveillance requirements.

Susceptibility testing

Four laboratories are still using CLSI methods and breakpoints (but they are all in various stages of changing to EUCAST). Expected susceptibility results follow.

NAC05: *Citrobacter freundii* complex **NDM-1**, CTX-M ESBL
NAC06: *E. coli* **OXA-48**, CTX-M ESBL
NAC07: *K. pneumoniae* **KPC-2**, CTX-M ESBL

EXPECTED RESULTS

	NAC05			**NAC06**			**NAC07**		
	***C. freundii* NDM-1/ESBL**			***E. coli* OXA-48/ESBL**			***K. pneumoniae* KPC-2/ESBL**		
ANTIBIOTIC	MIC	DISC	CATEGORY	MIC	DISC	CATEGORY	MIC	DISC	CATEGORY
Ampicillin	>16	0	R	>16	0	R	>16	0	R
Amox/Clavulanic acid	≥32/2	0	R	>32/2	8	R	>32/2	0	R
Cephalexin	>32	0	R	>32	0	R	>32	0	R
Cefuroxime	≥16	0	R	>16	0	R	>16	0	R
Cefoxitin	≥16	0	R	≤4	23	S	8	18	S - I
Ceftriaxone	≥4	0	R	>4	10	R	>4	0	R
Cefpodoxime	NT	0	R	NT	0	R	NT	0	R
Ceftazidime	≥32	0	R	4	19	I	>32	0	R
Piperacillin/Tazobactam	≥64/4	8	R	8/4	17	S (ATU)	64/4	12	R
Temocillin		0	R		9	R		0	R
Ertapenem	>2	12	R	0.5	24	S* (R)	>2	12	R
Imipenem	8	14	R	2	24	S*	2	18	S - I
Meropenem	8	15	I-R	≤0.125	26	S*	1	17	S - I

S* = raised MICs; resistant to erta by disc; mero screening cut-off