NZ NAC Education Bugs 2022

On behalf of the NZ NAC, thank you for participating in this exercise. It's great to see such universal engagement and cooperation amongst our clinical laboratories.

This year has been another challenging one for many labs, so we decided to send out only one set of bugs. This exercise consisted of 2 parts; the first part was to determine the ability of laboratories to accurately detect penicillin resistance in *Staphylococcus aureus*. The second part looked at antimicrobial reporting choices, based on a fully susceptible *E. coli*, if isolated from urine or blood cultures.

Staphylococcus aureus Penicillin Susceptibility Testing

This exercise was based on the recent SNAP (*Staph aureus* Network Adaptive Platform) study (an international study looking at different treatment options for *S. aureus* bacteraemia). Dr Susan Morpeth provided the following background information:

Patients with PSSA (penicillin-susceptible *S. aureus*) can be randomised between penicillin and flucloxacillin treatment.

Patients with MSSA (methicillin/cefoxitin-susceptible *S. aureus*) can be randomised between flucloxacillin and cephazolin treatment.

Patients with MRSA (methicillin/cefoxitin-resistant *S. aureus*) can be randomised between vancomycin and vancomycin plus cephazolin.

One of the key early decision points is whether patients have PSSA, MSSA or MRSA in their blood.

Eight isolates, consisting of 4 *S. aureus* strains [(S1/S6), (S2/S7), (S3/S5/S8), (S4)] were sent to 20 laboratories, including ESR:

Isolate #	*blaZ* PCR	*Expected penicillin result*
S1/S6	Positive	R
S2/S7	Negative	S
S3/S5/S8	Positive	R
S4	Positive	R

Labs were asked to perform penicillin disc diffusion and to record the zone size and to describe if the zone was fuzzy/beached or raised/sharp. As per EUCAST, a zone of ≥ 26mm together with a fuzzy/beached edge is considered susceptible; however, if the zone is <26mm or ≥ 26mm but the edge is raised or sharp, it is considered resistant. The presence of *blaZ* in *S. aureus* confers penicillin resistance via the production of penicillinase but can be difficult to detect reliably in the lab.

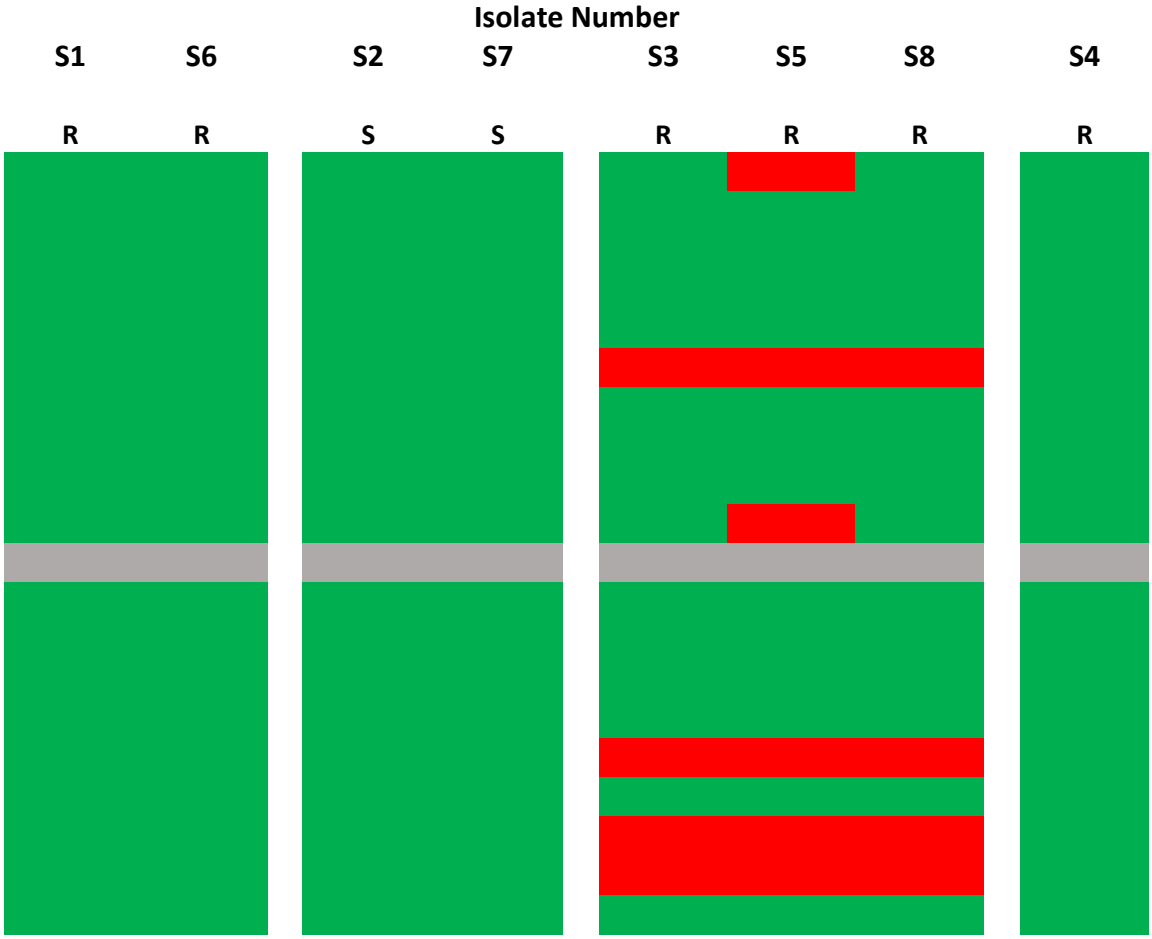
Results:

18 laboratories returned disc diffusion zone sizes, all used penicillin 1-unit discs based on EUCAST guidelines. Two labs did not return disc diffusion zone sizes; one lab performed testing by Vitek only as they do not confirm penicillin susceptible *S. aureus* or report the penicillin result. One lab stated that they had already completed the SNAP study and had achieved correct results for that, but they did not supply those results.

Automated analysers

Eight labs have automated analysers (4 Vitek, 4 Phoenix), but only 5 labs were able to supply analyser results. As expected, the analyser results revealed very major errors (VMEs) for all isolates harbouring *blaZ* [(S1/S6), (S3/S5/S8), (S4)], incorrectly classifying all these isolates as susceptible. See Table 1.

Disc Diffusion results



a. Did not participate in this study but achieved the correct results for the SNAP study

b. Laboratory does not perform penicillin disc diffusion

Correct category result

Incorrect category result (VME)

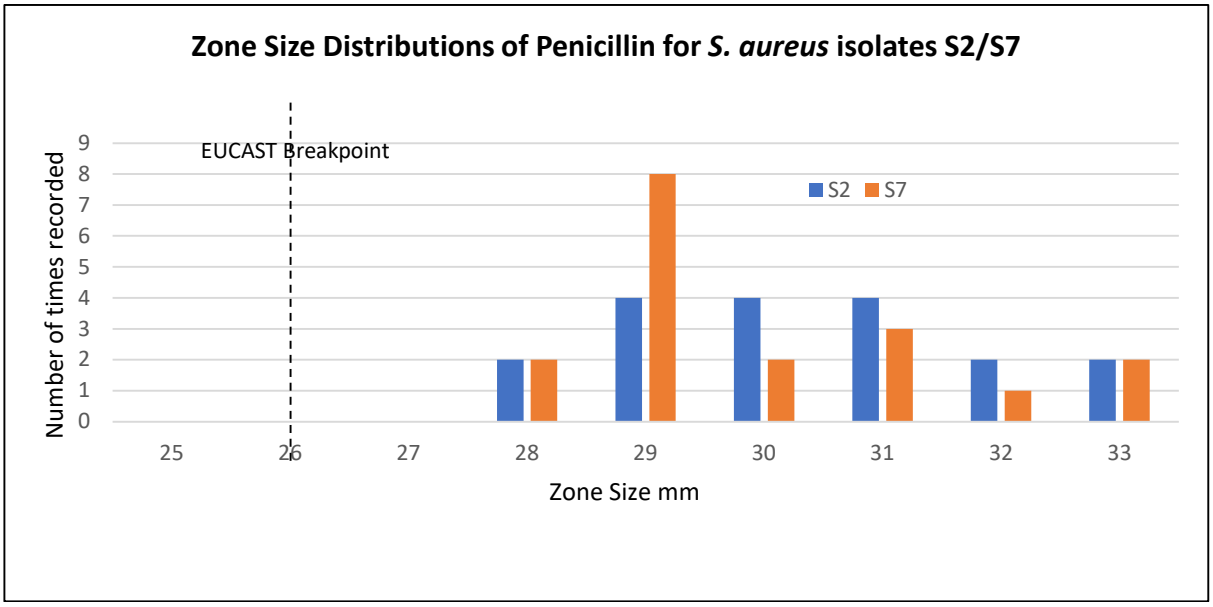
Analyser	Isolate Number S1	S6	S2	S7	S3	S5	S8	S4
Expected result	R	R	S	S	R	R	R	R
Vitek	0.06	0.06	0.12	0.06	0.06	0.12	0.06	0.12
Vitek	0.03	0.06	0.06	0.06	0.03	0.03	0.03	0.06
Vitek	0.06	0.06	0.12	0.12	0.06	0.12	0.06	0.06
Vitek	0.06	0.06	0.06	0.12	0.06	0.06	0.06	0.03
Phoenix	0.125	0.125	0.125	0.125	0.125	0.125	0.125	0.125
Phoenix x3	No panels available or only performed if isolated from blood cultures							

Table 1

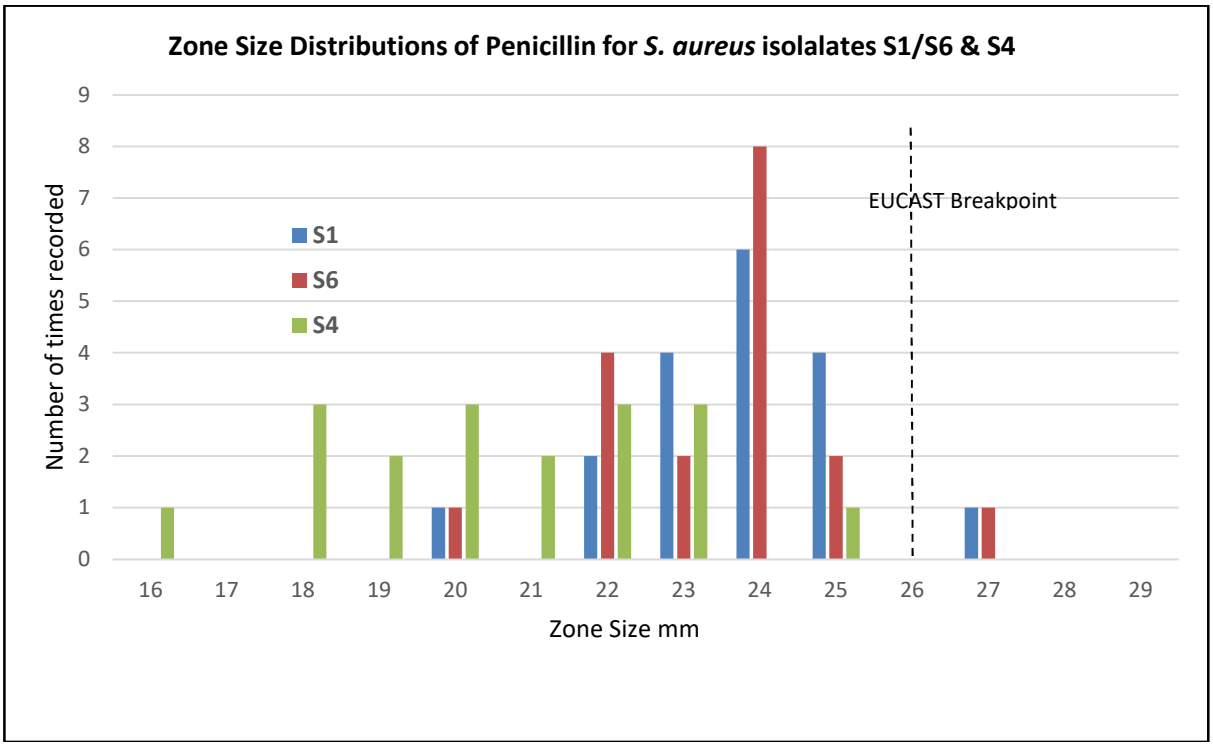
Disc diffusion

Susceptibility testing performed by disc diffusion was superior for most isolates.

Isolates S2/S7 were penicillin susceptible (*blaZ*/beta-lactamase negative) with fuzzy/beached edges and produced large zones in the 28mm-33mm range, with nearly 70% of the results having zones between 29-31mm. There was 100% concordance with these isolates.

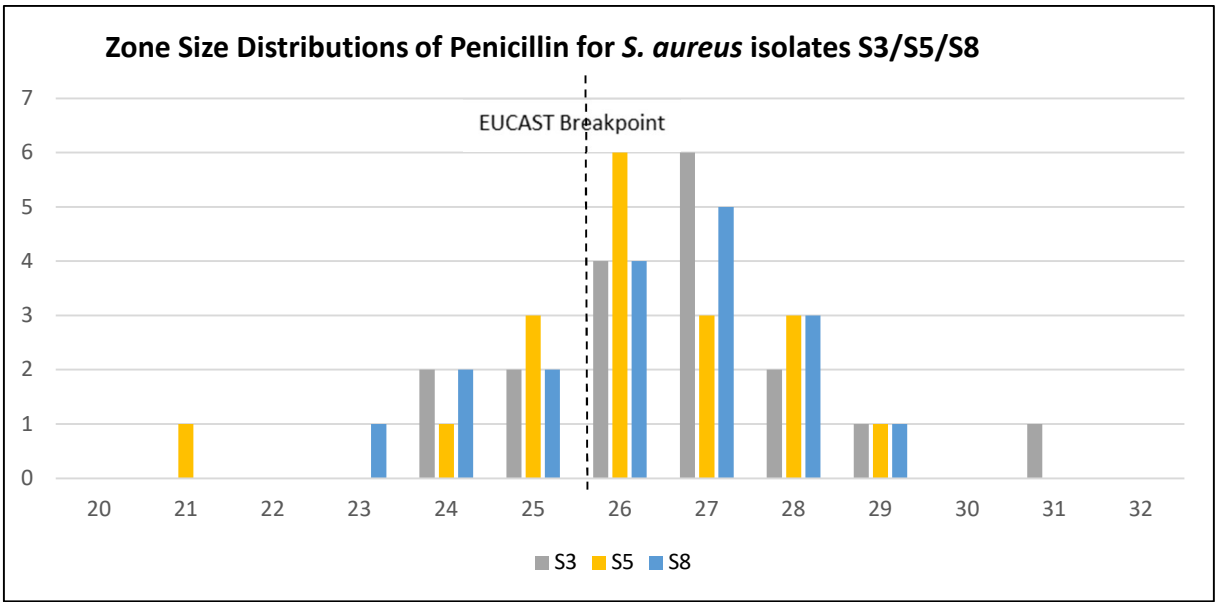


Isolates S1/S6 and S4 were penicillin resistant, with reported zones ranging from 20-27mm for S1/S6 and 16-25mm for S4. Despite the surprisingly large variation in zone sizes, all labs reported a raised edge and correctly classified these isolates as resistant, including zones recorded as 27mm.



Isolates S3/S5/S8 were responsible for all the VMEs. They were the same tricky strain in triplicate – all nutrient agar slopes were inoculated from a single blood agar purity plate, on the same day. Zone sizes ranged from 21-31mm. Incredible that the same bug, using the same methodology, can produce zone sizes with a 10mm difference! Most labs reported zones clustered around the

breakpoint. All incorrect results had zones in the 26-28mm range. Interestingly, the 3 recordings of 29mm (all from the same lab) and the one 31mm, all had raised edge and were correctly classified as resistant. One lab recorded 27mm for all 3 isolates and described a raised edge but failed to reclassify the results as resistant. All remaining incorrect results were associated with a fuzzy edge.



Conclusion:
This exercise has shown that the EUCAST disc diffusion penicillin 1-unit method has good correlation with the detection of penicillin resistance and that the majority of labs performed well. In contrast, automated methods such as Vitek and Phoenix are not reliable, resulting in a high level of VMEs. Laboratories need to have a heightened awareness of the zone edge, particularly with zones ≥26mm. Confirmation of penicillin resistance could be performed by PCR detection of *bla*Z; however, this test does not seem to be widely available in NZ, so a cautious approach would be to classify the isolate as resistant, or not releasing the penicillin result to the clinician.

Antimicrobial Reporting

The second part of this exercise was designed as a follow up to "**The New Zealand Guideline for Reporting of Antimicrobials in Microbiology Laboratories**." See publication by Juliet Elvy (*Elvy J. The New Zealand Guideline for Reporting of Antimicrobials in Microbiology Laboratories: an opportunity for laboratory based antimicrobial stewardship activities in New Zealand. New Zealand Journal of Medical Laboratory Science. 2021 Aug;75(2):90-108.*)

Labs were provided with a spreadsheet detailing zones sizes and MIC values for a fully susceptible *E. coli* and asked to tick which antibiotics the lab has available for testing, and which antibiotics would be **routinely reported** to the clinician/GP/ward if the isolate was recovered from a urine or from blood cultures.

All 19 laboratories completed this section (ESR not applicable). All labs reported a good range of testing capabilities:

Antibiotics tested	Number
Ampicillin/Amoxicillin	19
Amoxicillin-clavulanic acid	19
Ceftriaxone	19
Ciprofloxacin	19
Gentamicin	19
Meropenem	19
Nitrofurantoin	19
Trimethoprim	19
Trimethoprim-sulfamethoxazole	19
Piperacillin-tazobactam	18
Cefoxitin	17
Ceftazidime	17
Cefuroxime	17
Ertapenem	15
Cefalexin/Cefaclor	14
Cefepime	14
Aztreonam	9
Norfloxacin	9
Imipenem	6

Urine reporting

Most labs indicated that they report narrow spectrum, or first-line, antimicrobials, including Ampicillin/Amoxicillin, Cefalexin/Cefaclor, Nitrofurantoin, Trimethoprim (some labs indicating they would also report Trimethoprim-sulfamethoxazole on children):

Antibiotics reported in URINE	**Number**
Ampi/Amox	19
Nitrofurantoin	19
Trimethoprim	19
Gentamicin	14
Cefalexin/Cefaclor	13
Trimethoprim-sulfamethoxazole	9
Amoxicillin-clavulanic acid	5
Cefuroxime	5
Norfloxacin	1

The total number of antibiotics reported ranged from 3 to 8, with 84% of laboratories reporting 6 or fewer antibiotics. For a fully susceptible *E. coli*, the guidelines recommend reporting Ampi/Amox, Cefalexin/Cefaclor, Nitrofurantoin and Trimethoprim for community patients and adding a narrow spectrum IV antimicrobial such as cefuroxime and/or gentamicin for hospital patients. *E. coli* susceptible to ampicillin should have amoxicillin-clavulanic acid suppressed. Pleasingly, only one lab reported a quinolone (norfloxacin) for this fully susceptible *E. coli* from urine – this outlying lab may wish to review their processes.

Blood culture reporting

18/19 laboratories completed this section (one laboratory does not do B/Cs). Overall there was excellent compliance to the guidelines, with only a couple of labs reporting more than 5 antibiotics (range 3 to 7 antibiotics reported):

Antibiotics reported in BLOOD	Number
Ampi/Amox	18
Gentamicin	17
Trimethoprim-sulfamethoxazole	16
Cefuroxime	14
Ceftriaxone	6
Amoxicillin-clavulanic acid	5
Ciprofloxacin	2
Meropenem	1
Tobramycin	1

A few labs indicated that they would add the EUCAST comment "*For systemic infections, aminoglycosides should be used in combination with other active therapy*" if reporting gentamicin. One laboratory co-reported tobramycin and one laboratory reported meropenem. For cefuroxime, most labs indicated that they would either report as "I" or add a comment regarding appropriate dosing. The NZ reporting guidelines indicate Ampi/Amox, Gentamicin, Trimethoprim-sulfamethoxazole, and Cefuroxime – although some labs are also reporting Ceftriaxone due to empirical use in patients with suspected sepsis. The outlying labs reporting ciprofloxacin or meropenem for this fully-susceptible *E. coli* may wish to review their processes.

Conclusion:

Most laboratories are adhering to the antibiotic reporting principles as set out in The New Zealand Guideline for Reporting of Antimicrobials in Microbiology Laboratories. The guideline was developed by members of the NZNAC, with input and approval by NZMN members and the RCPA. We suggest that microbiologists are mindful of two important reporting strategies including only reporting the narrowest spectrum site-effective antimicrobial agents and not reporting broad-spectrum reagents such as quinolones, 3rd generation cephalosporins, piperacillin-tazobactam and carbapenems except when other equally efficacious treatment options are unavailable.