Strengthening Antimicrobial Resistance Surveillance through External Quality Assessment

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Introduction

Antimicrobial resistance (AMR) is increasing worldwide and is associated with significant morbidity and mortality. While laboratories strive to continually improve their capabilities in identifying AMR, programs dedicated to laboratory quality assessment (QA) of AMR are relatively new due to their complexities. In 2021, the Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) introduced an External QA (EQA) program for multi-drug-resistant (MDR) Gram-negatives (Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*). This was further expanded in 2024 to include some additional AMR organisms of concern recognised by the Australian National Alert System for Critical Antimicrobial Resistance (CARAlert) and by the World Health Organisation (WHO)[1,2]. The program has seen much interest, with significant enrolments in the Asia-Pacific region.

Table 1 Australian National Alert System for Critical Antimicrobial Resistance (CARAlert) list and nationwide statistics for 2024.[3] Highlighted are the items included in the EQA Program.

Organism	Critical Resistance	N = (2024) up to 30 September 2024	Relative change (%) from 2023 to 2024
Acinetobacter baumannii cx.	Carbapenemase producing	33	▲ 18
Enterobacterales	Carbapenemase producing	1068	▲ 30
Pseudomonas aeruginosa	Carbapenemase producing	55	▲ 2
Salmonella spp.	ESBL producing	67	▼ 6
Shigella spp.	Multidrug - Resistant	263	▼ 33
Enterococcus spp.	Linezolid - Resistant	88	▲193
Candida auris	–	12	▼ 12
Organisms included in the EQA from 2021 – 2024 (Figures 2a & 2b) Organisms included in the EQA from 2024 (Figures 3a & 3b)			

Objective

Review and summarise laboratory performance in the AMR EQA module and discuss participants' proficiency and the benefits of a well-established EQA in strengthening the surveillance of AMR.

Method

The RCPAQAP provides lyophilised material to almost one hundred participants worldwide, containing organisms already characterised for phenotypic and genotypic resistance, through referral to reference laboratories external to the RCPAQAP. Items are stringently quality-tested for homogeneity and stability before dispatch and require rehydration prior to processing. Laboratories are provided with a clinical note for each item relevant to sample processing and are expected to perform testing in accordance with their standard operating procedures. Results are submitted using the RCPAQAP online portal and are scored according to concordance with expected results (Table 2). Laboratories are encouraged to indicate their testing methods employed for each item. Submitted results from participating laboratories since 2021 were reviewed in this report, with key findings highlighted below.

Table 2 The RCPAQAP Microbiology Assessment Guide

RCPAQAP Assessment Grading	Based on the Performance
Concordant	A result containing the target organism or the expected result
Discordant	A result that is substantially different from the expected or target result
Not Assessed	Test not performed by the participant; Participant has referred the item for further testing; The result is beyond the scope of acceptance for grading.

Results

- Most clinical microbiology laboratories use a combination of phenotypic and molecular AMR identification methodologies alongside screening media and antimicrobial susceptibility testing (AST)[4]. Approx. 20% relying solely on screening media and/or AST data (Figure 1).
- Laboratories achieved >80% concordance for susceptible and Extended Spectrum β-lactamase (ESBL) positive organisms (Figures 2a and 2b). ESBL containing *Salmonella* Typhimurium and *Shigella sonneii* were exceptions, with less than 80% concordance (Figures 3a and 3b).
- Laboratories were consistently more able to identify common class A and B β-lactamases, such as bla_{KPC}, bla_{NDM}, bla_{VIM}, and bla_{IMP} in Enterobacterales (Figures 2a and 2b).
- The detection and reporting of the class D β-lactamase, $bla_{OXA-48-like}$, in *Escherichia coli* have improved between 2021 and 2023 (Figure 2b), whilst interpretation for other resistance mechanisms remained relatively unchanged (Figure 2b).
- Notably, poor performance in the identification of $bla_{OXA-23-like}$ and bla_{GES-5} in *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, respectively (Figure 2a). However, an improvement was observed in the interpretation of *A. baumannii* harbouring $bla_{OXA-23-like}$ (Figure 2b). These isolates remain a challenge for a large cohort of participants.
- A few laboratories could detect and report the presence of *Candida auris* or linezolid-resistant *Enterococcus faecium*, with 22% and 20% concordance for these items, respectively (Figures 3a and 3b).
- Participants achieved >90% concordance for interpreting vancomycin-resistant Enterococci (VRE) (Figure 3b), although only 60% could report the genotypic mechanism (Figure 3a).

AST: Antimicrobial Susceptibility Testing
NAAT: Nucleic Acid Amplification Test
mCIM: modified carbapenem inactivation method
NGS: Next Generation Sequencing

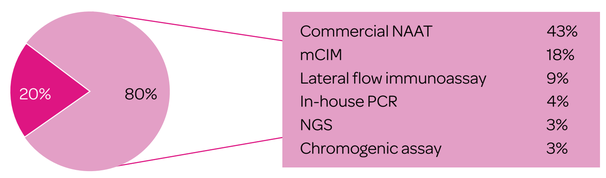

Figure 1 AMR Testing Methodologies Reported by the Participants

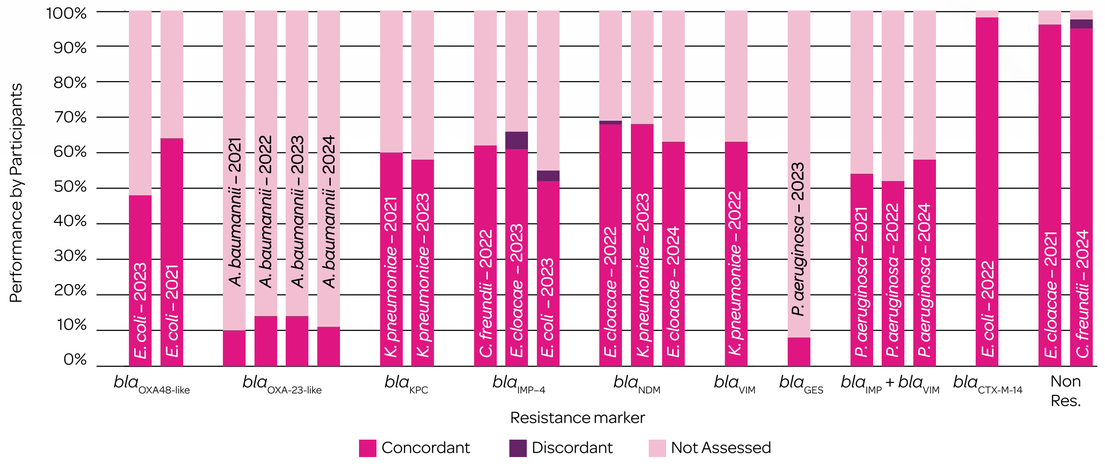

Figure 2a Agreement in Identifying the Mechanisms of Genotypic Resistance (2021–2024)

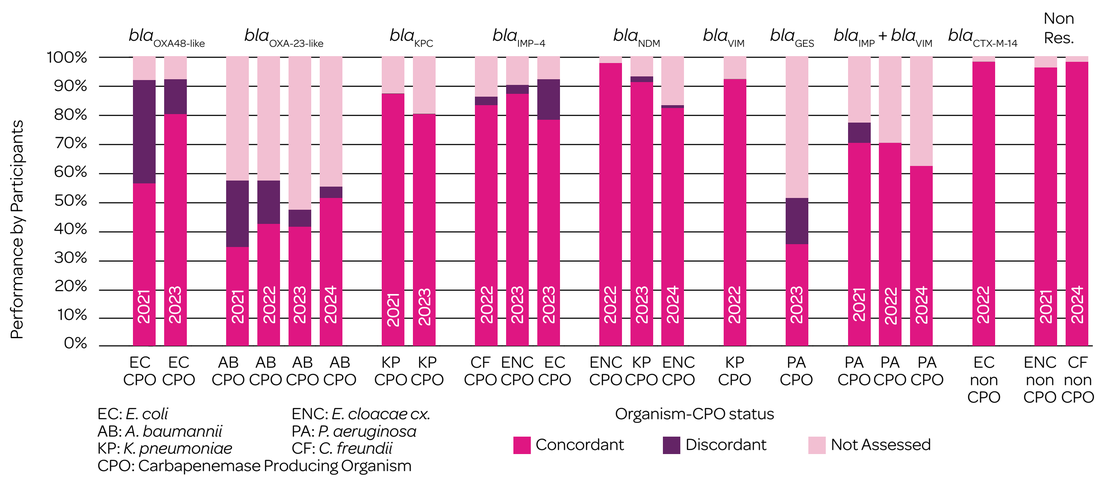

Figure 2b Agreement in Reporting Overall Interpretation of Phenotypic/Genotypic Resistance (2021–2024)

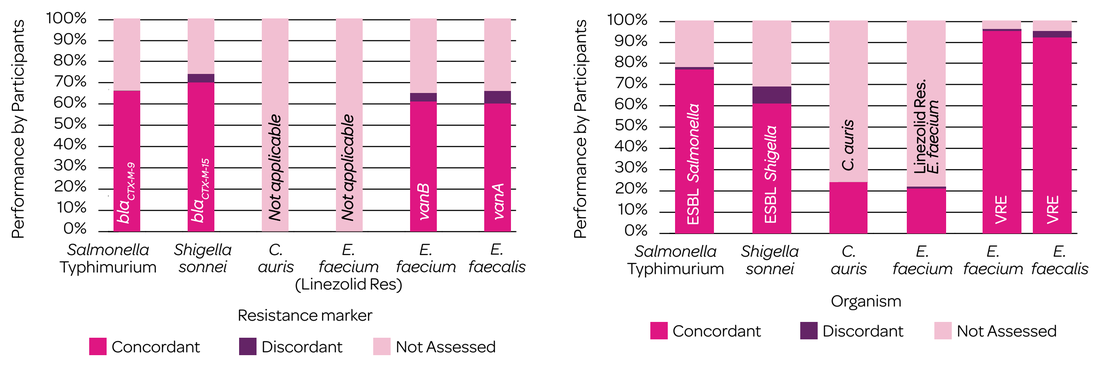

Figure 3a Agreement in Identifying the Mechanisms of Genotypic Resistance in Organisms Included Since 2024

Figure 3b Agreement in the Overall Interpretation of Phenotypic/Genotypic Resistance in Organisms Included Since 2024

Discussion

- The RCPAQAP AMR EQA module has demonstrated high-quality performance in the detection of common β-lactamases in most Enterobacterales. However, performance requires improvement for the detection/interpretation of other organisms and less common resistance markers.
- Many testing methodologies have drawbacks in detecting carbapenemase production in *P. aeruginosa* and *A. baumannii*, which remains challenging for some laboratories.
- Most laboratories do not rely solely on a phenotypic/molecular methodology for the interpretation of AMR in their testing algorithm. e.g. Approx. 80% use screening media, AST (Diagnostic disks or BMD) and the mCIM test as supplementary testing methods.
- A significant proportion relies on the referral of isolates to a third-party laboratory for confirmation, as evidenced by the proportion of not assessed results. Delays in confirmation and/or reporting for genuine patient samples may lead to delays in appropriate clinical management and infection prevention practices.
- Laboratories should refer isolates with indeterminate resistance mechanisms to first- and last-line therapies to reference laboratories with the capacity to perform advanced molecular screening assays or NGS.
- While the heightened detection of vancomycin-resistant Enterococci (VRE) is well confirmed, laboratories must improve the screening of emerging AMR pathogens and determine their resistance mechanisms.

Conclusion

- EQA has an essential role in the quality of AMR detection and reporting and modules can be designed to assist improvements in laboratory practices to support global antimicrobial stewardship efforts and rising rates of AMR.
- This system ensures that laboratories follow standard protocols, minimise errors, and enhance the overall understanding of antimicrobial resistance trends locally and globally.
- Through regular proficiency testing, training, and feedback, EQA providers such as the RCPAQAP provide laboratories with the tools they need to improve their testing processes and identify the strengths and weaknesses of their assigned AMR procedures.
- RCPAQAP will strive to continuously improve EQA in AMR for laboratories by providing challenging isolates with novel/rare resistance markers in addition to those more commonly encountered in the diagnostic laboratory.

References

1. WHO Bacterial Priority Pathogens List 2024. Geneva: World Health Organization; 2024.
2. Australian Commission on Safety and Quality in Health Care. CARAlert Laboratory Handbook. Sydney: ACSQHC; 2022.
3. Australian Commission on Safety and Quality in Health Care. CARAlert data update 39: 1 July 2024–30 September 2024. Sydney: ACSQHC; 2024.
4. Kaprou, G. D. *et al.* (2023). Rapid Methods for Antimicrobial Resistance Diagnostics. *Antibiotics*. Vol. 10, 209.

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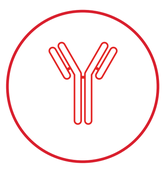

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