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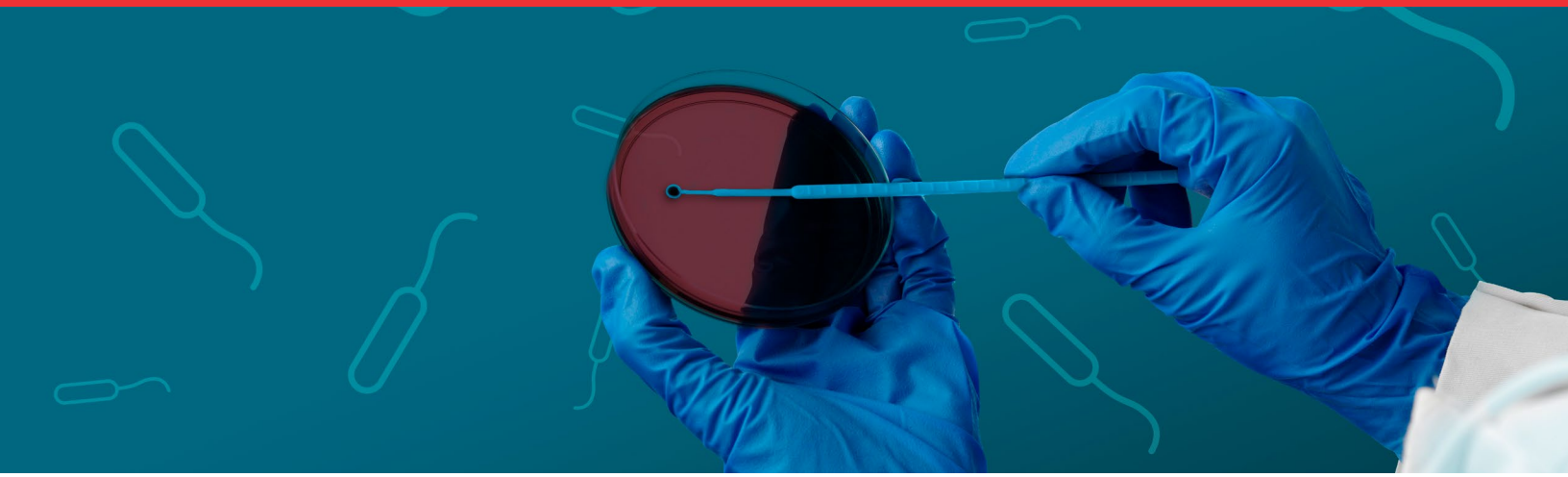

SMART NOTE

Quality Control for Antimicrobial Susceptibility Testing

Ensuring detection of novel antimicrobial resistant strains

Look out for Carbapenemases

The development of antimicrobial resistance is part of natural evolutionary process among microorganisms, delivering beneficial traits in bacteria that protect the cell from the effects of specific antibiotics, thus conferring a survival advantage. However, the increased use, and misuse, of antimicrobials promotes the accelerated spread of resistance mechanisms, leading to the development of multi and pan-resistant bacteria that are untreatable with the antibiotics currently in use[1]. The detection, correct diagnosis and treatment and surveillance of antimicrobial resistant organisms is key to fighting this growing global issue.

One mechanism of drug resistance, carbapenem resistance among Gram negative bacteria, has become significantly more prevalent since the 1990's[2]. Carbapenems (e.g. Meropenem, Imipenem, Ertapenem, Doripenem) are broad-spectrum β-lactam antibiotics traditionally used as drugs of last resort targeting healthcare-associated and severe community-acquired infections. The increasing prevalence of extended-spectrum β-lactamases (ESBL), enzymes conferring resistance to carbapenem antibiotics by breaking/hydrolysis of their structure, among *Escherichia coli* and *Klebsiella pneumoniae* in 1980s-1990's contributed to increased consumption of Carbapenems, which in turn prompted the evolution of various mechanisms of carbapenem resistance[3], detailed here:

- Carbapenemase (enzymes hydrolysing carbapenem antibiotics) production (e.g. KPC*, NDM*, VIM*, IMP*, OXA-48*)[3, 4, 5]
- Loss or alteration of outer membrane porins[3, 4]
- Augmented drug efflux[3, 4]
- Alterations in penicillin binding proteins [3, 4, 6]
- β-lactamase activity (eg. AmpC*, SHV*, TEM*, CTX-M* β-lactamases) combined with structural mutations (loss of porins, efflux systems) [4, 5]

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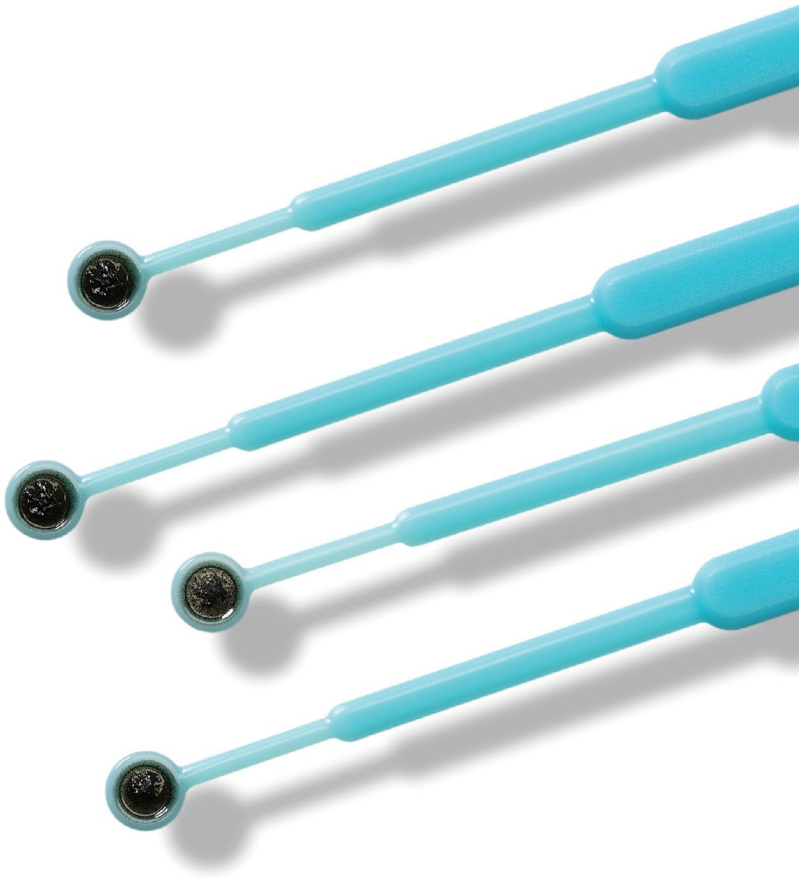
The prevalence of different carbapenem resistance mechanisms varies geographically with *Klebsiella pneumoniae* carbapenemases (KPC) being the most prevalent in the Americas and parts of Europe, metallo-β-lactamases (eg. NDM, VIM, IMP) most prevalent in Asia and OXA-48-like resistance being highest around the Mediterranean area and the Middle East[4, 7, 8]. Of particular concern is the spread of KPC producing *Klebsiella pneumoniae* which is one of the most common types of carbapenem resistant Gram negative bacteria[9]. *K. pneumoniae* is a major cause of hospital-acquired infections such as pneumonia, bloodstream infections and UTI, and KPC infections are currently associated with mortality rates as high as 41%[9, 10].

The international spread of KPC producing Enterobacterales is primarily due to clonal expansion of *K. pneumoniae* strains harbouring KPC coding genes (bla_{KPC}) which are often located in a transposon or a plasmid enabling rapid dissemination of these genes among Enterobacterales[4, 5, 11]. The level of carbapenem resistance, measured as minimum inhibitory concentration (MIC) value, has been discovered to be linked to bla_{KPC} gene copy number[4].

As the fight to control multi-drug resistant organisms continues, it is of upmost importance to ensure antimicrobial susceptibility testing (AST) solutions can recognize different resistance patterns through antibiograms in order to guide effective patient treatment. The accuracy and reliability of a chosen AST system to detect antimicrobial resistance present in a clinical isolate should be evaluated through in vitro analysis using characterized microbial strains with known antibiotic susceptibility profiles, as part of routine Quality Control (QC) testing.

Guidelines by CLSI[12] and EUCAST[13] are continuing to evolve as more and more antimicrobial resistant QC strains are added into routine QC recommendations. Best practice QC is of particular relevance for those strains with plasmid mediated resistance (such as KPCs) that are prone to spontaneous plasmid loss due to over-passaging. By following best practice guidance on QC strain maintenance – avoiding over-passaging and maintaining optimal storage and growth conditions - laboratories can ensure proper handling of these strains[12].

Thermo Scientific™ Culti-Loops™ include carbapenem resistant *Klebsiella pneumoniae* strains ATCC® BAA-2814™ and ATCC® BAA-1705™. View the latest additions to the Thermo Scientific Culti-Loops portfolio here, to gain access to the full, ready-to-use QC strains according to recommendations by CLSI and EUCAST. All Culti-Loops strains are fully characterised, including those harbouring a variety of antimicrobial resistance patterns such as ESBL & Carbapenemase producing strains, Vancomycin-Resistant Enterococci (VRE) and Methicillin-Resistant *Staphylococcus aureus* (MRSA).



*KPC: Klebsiella pneumoniae carbapenemase-producing Enterobacterales; NDM: New Delhi metallo-β-lactamase; VIM: Verona integron-encoded metallo-β-lactamase; IMP: Imipenem-resistant Pseudomonas-type carbapenemase; OXA-48: carbapenem-hydrolysing oxacillinase-48; AmpC: ampicillinase C; SHV: sulfydryl variant; TEM: Temoneira; CTX-M: cefotaximase.

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References

1. World Health Organization, 2020. Antimicrobial resistance, Key facts, 13 Oct 2020. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance
2. Gupta, N. et al. Carbapenem-Resistant Enterobacteriaceae: Epidemiology and Prevention. Clinical Infectious Diseases, Volume 53, Issue 1, 1 July 2011, Pages 60–67, https://doi.org/10.1093/cid/cir202 https://academic.oup.com/cid/article/53/1/60/492128
3. Patel, G. & Bonomo R.A. "Stormy waters ahead": global emergence of carbapenemases. Front Microbiol. 2013; 4: 48. Published online 2013 Mar 14. doi: 10.3389/fmicb.2013.00048 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3596785/
4. Logan, L.K. & Weinstein R.A. The Epidemiology of Carbapenem-Resistant Enterobacteriaceae: The Impact and Evolution of a Global Menace. J Infect Dis. 2017 Feb 15; 215(Suppl 1): S28–S36. Published online 2017 Mar 28. doi:10.1093/infdis/jiw282 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5853342/
5. Pitout, J.D.D. et al. Carbapenemase-Producing Klebsiella pneumoniae, a Key Pathogen Set for Global Nosocomial Dominance. Antimicrob Agents Chemother 2015 Oct;59(10):5873-84. doi: 10.1128/AAC.01019-15. Epub 2015 Jul 13. https://pubmed.ncbi.nlm.nih.gov/26169401/
6. Dhruvitkumar, S.S. et al. First Penicillin-Binding Protein Occupancy Patterns of β-Lactams and β-Lactamase Inhibitors in Klebsiella pneumoniae. Antimicrob Agents Chemother. 2018 Jun; 62(6): e00282-18. Published online 2018 May 25. doi: 10.1128/AAC.00282-18 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5971569/
7. Van Duin, D. & Doi, Y. The global epidemiology of carbapenemase-producing Enterobacteriaceae. Virulence. 2017; 8(4): 460–469. Published online 2016 Aug 11. doi: 10.1080/21505594.2016.1222343 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5477705/
8. Pitout, J.D.D. et al. The Global Ascendency of OXA-48-Type Carbapenemases. Clin Microbiol Rev. 2019 Nov 13;33(1):e00102-19. doi: 10.1128/CMR.00102-19. Print 2019 Dec 18. https://cmr.asm.org/content/33/1/e00102-19
9. Tsioutis, C. et al. Transmission of Klebsiella pneumoniae carbapenemase (KPC)-producing Klebsiella pneumoniae: the role of infection control. Journal of Antimicrobial Chemotherapy, Volume 76, Issue Supplement_1, January 2021, Pages i4–i11, https://doi.org/10.1093/jac/dkaa492 https://academic.oup.com/jac/article/76/Supplement_1/i4/6127048
10. Bedenic, B. et al. Klebsiella pneumoniae carbapenemase (KPC) in urinary infection isolates. Arch Microbiol. 2021 Jan 28. doi: 10.1007/s00203-020-02161-x. https://pubmed.ncbi.nlm.nih.gov/33507339/
11. Schultsz, C. & Geerlings, S. Plasmid-mediated resistance in Enterobacteriaceae: changing landscape and implications for therapy. Drugs 2012 Jan 1;72(1):1-16. doi: 10.2165/11597960-000000000-00000. https://pubmed.ncbi.nlm.nih.gov/22191792/
12. The clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial susceptibility Testing. 30th ed. CLSI supplement M100. Clinical and Laboratory Standards Institue, USA, 2020.
13. The European Committee on Antimicrobial Susceptibility Testing. Routine and extended internal quality control for MIC determination and disk diffusion as recommended by EUCAST. Version 11.0, 2021. http://www.eucast.org

To find out more about QC for Antimicrobial susceptibility testing system, visit **thermofisher.com/QCforAST**

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