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Evaluation of a Molecular Syndromic Panel for Detection of Bacteria and Resistance Markers in Positive Blood Cultures

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Introduction

Rapid and accurate identification of organisms in positive blood cultures is integral to patient care. Supply chain issues with the standard of care (SOC) molecular blood culture identification (BCID) assays in use at the Johns Hopkins Microbiology Laboratory (GenMark ePlex BCID-GP, BCID-GN panels) prompted an evaluation of the bioMerieux BioFire BCID-2 panel. This study evaluated the two molecular blood culture syndromic panel tests for rapid identification of Gram-positive and Gram-negative organisms and antimicrobial resistance (AMR) markers in positive blood cultures.

The BioFire BCID-2 panel tests for 43 Gram-positive, Gram-negative and yeast organisms and AMR markers. We did not evaluate yeast detections in this study. BioFire BCID-2 results in ~1 hour.

The ePlex BCID panels are separated into two cartridges: BCID-GP tests for 24 Gram-positive organisms and AMR markers and BCID-GN tests for 27 Gram-negative organisms and AMR markers. Eplex BCID-GP and BCID-GN result in ~1.5 hours.

Figure 1 is an example of a BioFire FilmArray test cartridge.

Figure 1: BioFire FilmArray Test Cartridge
https://www.biofiredx.com/products/solutions/point-of-care/

Methodology

Testing was performed following manufacturers' recommendations for both molecular platforms. Off-panel organisms were identified using the Bruker Biotyper MALDI-TOF MS instrument software version 3.2.14/16 (Claim 6) from solid media growth. Antimicrobial susceptibility testing was performed as part of SOC. Over a 60-day period, we tested 133 prospective clinical samples aiming to test at least 2 positive blood cultures per panel target. Inclusion of 19 contrived samples ensured evaluation of low prevalence targets and challenged AMR marker detection. 10 uninoculated blood culture broths were also included. Overall positive percent agreement (PPA) and negative percent agreement (NPA) were calculated compared to SOC.

Summary of Evaluation by On-Panel BCID-2 Targets		
Enterococcus faecalis		6
Enterococcus faecium		2
Listeria monocytogenes		2
Staphylococcus spp.		11
Staphylococcus aureus		6
Staphylococcus epidermidis		5
Staphylococcus lugdunensis		3
Streptococcus spp.		8
Streptococcus agalactiae (Group B)		3
Streptococcus pneumoniae		2
Streptococcus pyogenes (Group A)		4
Staphylococcus epidermidis - 6	*mecA/C*	7
Staphylococcus lugdunensis - 1		
Staphylococcus aureus	*mecA/C* and MREJ (MRSA)	4
Enterococcus faecalis - 2	*vanA/B*	4
Enterococcus faecium - 2		
Acinetobacter calcoaceticus-baumannii complex		5
Bacteroides fragilis		3
Haemophilus influenzae		1
Neisseria meningitidis (encapsulated)		2
Pseudomonas aeruginosa		4
Stenotrophomonas maltophilia		2
Enterobacterales		3
Enterobacter cloacae complex		4
Escherichia coli		9
Klebsiella aerogenes		2
Klebsiella oxytoca		3
Klebsiella pneumoniae group		8
Proteus spp.		5
Salmonella spp.		2
Serratia marcescens		3
Escherichia coli - 6	CTX-M	11
Klebsiella pneumoniae group - 4		
Proteus spp. - 1		
Enterobacter cloacae complex - 1	KPC	2
Proteus spp. - 1		
Pseudomonas aeruginosa	IMP	1
Klebsiella oxytoca - 1	NDM	2
Salmonella spp. - 1		
Klebsiella aerogenes - 1	OXA-48-like	2
Klebsiella pneumoniae group - 1		
Pseudomonas aeruginosa - 1	VIM	2
Enterobacter cloacae complex - 1		
Escherichia coli	*mcr-1*	2

Figure 2: Chart Summarizing BCID-2 Targets Evaluated

Results

A total of 89 Gram-positive (67 on-panel, 22 off-panel) and 89 Gram-negative targets (78 on-panel, 11 off-panel) were assessed. Based on analysis of the 119 samples run with BCID-2 on-panel targets, PPA and NPA between BCID-2 and SOC were 98% and 100%, respectively. Overall, there were 2 missed on-panel BCID2 targets: one sample resulted as *Streptococcus anginosus* group by SOC (detected by ePlex BCID) while a second sample resulted as *Klebsiella pneumoniae* group (ESBL producer), *Klebsiella oxytoca/Raoultella* spp (Carbapenemase producer), *Stenotrophomonas maltophilia* by standard of care but *Stenotrophomonas maltophilia* was missed by both ePlex BCID and BCID2. 33 patient samples positive for off-panel targets and the 10 uninoculated broths all tested negative. BCID-2 detected all 15 Gram-positive and 22 Gram-negative AMR markers verified by SOC. 22 patient samples were polymicrobial and of those 14/22 (64%) had at least one target that was missed by ePlex BCID and detected by BCID-2. The invalid rate of ePlex BCID hovered between 5-10% in contrast to zero invalid tests with BioFire.

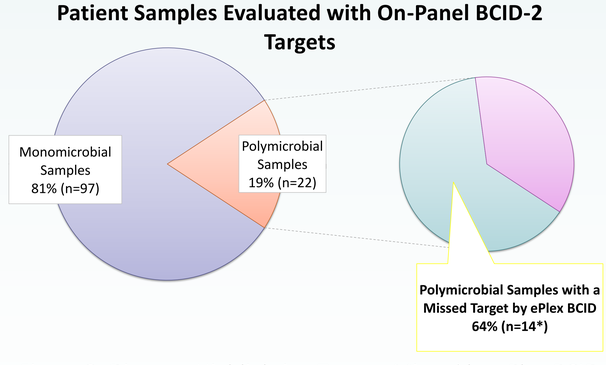

Figure 3: Diagram Highlighting Targets Missed by ePlex BCID in Polymicrobial Samples
*14 Eplex BCID samples with missed targets including: *A. baumannii, B. fragilis, Citrobacter* spp., *E. coli, E. faecalis, K. oxytoca, P. mirabilis, S. aureus, S. epidermidis, S. maltophilia, Streptococcus* spp., CTX-M, *mecA,* Pan-GP(3), Pan-GN.

Conclusion

The BCID-2 compared favorably to the ePlex BCID-GP and BCID-GN panels with high accuracy for on-panel targets and a much lower invalid rate. It was superior in performance to ePlex BCID for detection of polymicrobial samples.

Eplex BCID-GP and BCID-GN panels offer an additional 15 targets that are not tested for on the BioFire BCID-2 panel. Most of these targets can be classified as potential blood culture contaminants. Identifying potential contaminants can be crucial for antimicrobial stewardship related to positive blood cultures.

Switching platforms resulted in an estimated cost savings of $26,300.

- Baseline annual savings from reduced reagent cost of BCID-2
- More comprehensive BCID-2 obviated the need for 2 panels for polymicrobial samples
- Reduction in invalid rates with BCID-2

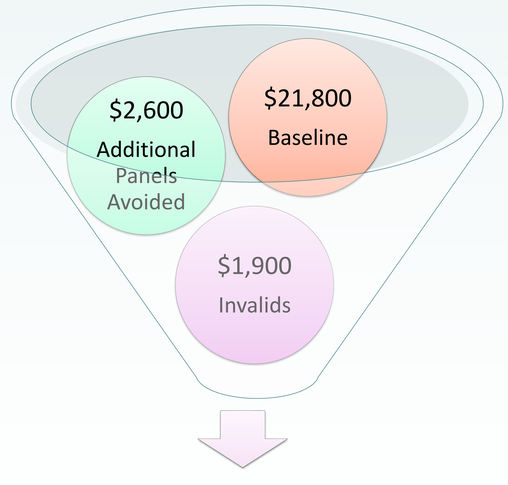

Figure 4: Visualization of Annual Cost Savings at JHH