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Evaluation of the Research Use Only Rapid Sample to Answer Blood Culture Identification Panels

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Introduction

Butler Memorial Hospital is a 296 bed health care facility located in Butler, Pennsylvania. The current turnaround time for a blood culture identification (ID) not only presents a challenge for providing a timely result to the team managing the patients care but also affects treatment, including appropriate use of antibiotics. We sought to evaluate the ePlex® Research Use Only (RUO) Blood Culture Identification Panels to compare them to our current methodology (Vitek 2®, bioMérieux) for accuracy and turnaround time. The panels, (BCID-GN, GP, and FP), which identify 15 fungal pathogens (BCID-FP), 20 Gram positive organisms (BCID-GP), and 21 Gram negative organisms (BCID-GN), including multiple resistance genes were found to cover all of the most common and significant organisms that we see at our facility.

Methods

A total of 107 de-identified positive blood cultures were evaluated during the study, compared to the laboratory standard of care (SOC) for ID and antimicrobial susceptibility testing (AST). The Gram stain result was used to determine the appropriate BCID Panel. The time to result is 1.5-2 hours from a positive blood culture. Discordant results were re-tested on each method one additional time and additional resolutions was done by PCR/Sequencing.

- Cartridges were provided by GenMark Diagnostics
- The ePlex BCID Panels are now FDA Cleared

Results

- 91.7-98.6% reduction in TAT from positive blood culture to ID/AST (See Figure 1) of ID and AMR (antimicrobial resistance gene) for ePlex (~ 90-100 min) compared to the SOC (24-144 hrs).
- A total of 107/113 organisms and 14 AMR were detected in the study. (See Table 1)
- 59 samples were tested with BCID-GP in which 2 identifications were missed by SOC. The ePlex BCID-GP correctly identified 1 *S. epidermidis* and 1 *Streptococcus anginosus* missed by culture and 1 *S. epidermidis* misidentified as *S. lugdunensis*. In one sample, ePlex BCID-GP did not detect *S. epidermidis* co-infected with *S. anginosus* group, which detected upon repeat of a new cartridge.
- 44 samples were tested with BCID-GN in which 2 identifications were missed by SOC. The ePlex BCID-GN correctly identified two *K. oxytoca* in polymicrobial infections not recovered by culture. ePlex detected 2 *K. pneumoniae* and 1 *S. marcescens* that were not reproducible during retest. Additionally 1 *M. morganii* was identified by the manufacturer as a cartridge defect that was corrected in subsequent cartridge lots.
- In total, 14 polymicrobial infections were detected of which 2 were not detected by our standard of care.
- Four samples were available to test on the BCID-FP Panel, 2 of which accurately identified *C. albicans* and 2 true negative samples.
- Prevalence rate of resistant organisms by AST was 12.4%. ePlex correctly identified an AMR associated with all resistant pathogens in 7 *S. aureus* with *mecA* , 1 *E. faecium* with *vanA* and 6 ESBL organisms with CTX-M. (See Figure 2)

Figure 1: Change in Turn Around Time from Current Standard of Care to the ePlex BCID Panels

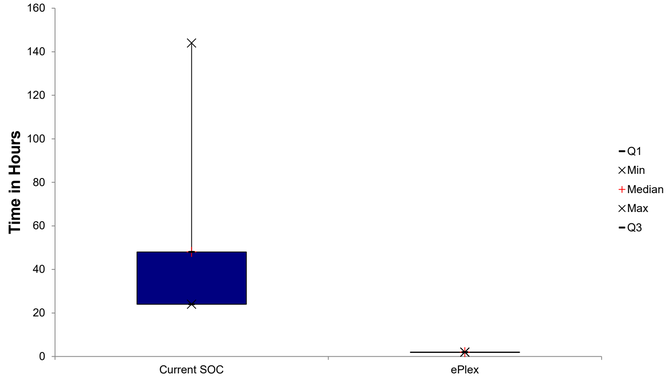
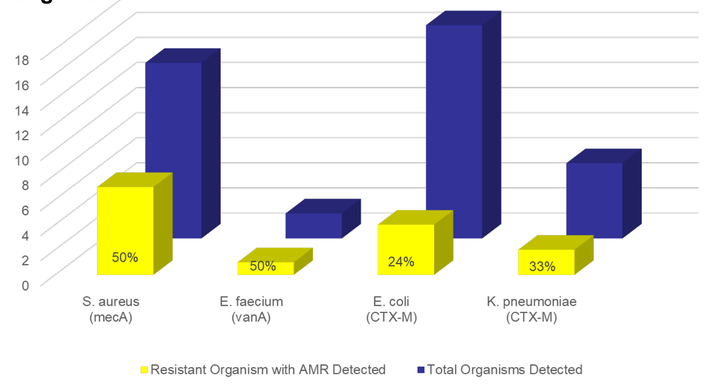


Figure 2: Confirmed Resistance Genes Detected by the ePlex BCID Panels Compared to the Overall Number of Detected Organisms



Theoretical Case Management	Reason and No. of Potential Interventions
Narrow Spectrum Antibiotic Escalation	AMR Detection = 1 VRE, 7 MRSA, 6 ESBL Potential MDRO Detection = 1 *S. maltophilia,* 3 *P. aeruginosa* Anaerobe Detection = 4 *B. fragilis,* 1 *F. nucleatum*
Broad Spectrum Antibiotic De-escalation	Gram Positive Contaminant = 1 *Corynebacterium*, 9 *S. epidermidis*, 2 *Staphylococcus* spp.
Isolation Change/Discharge Potential	12 GP Contamination, 14 AMR Detected

Table 1: Sensitivity and Specificity by Target Detected by the ePlex BCID Panels

ePlex BCID Panel	ePlex BCID Panel Targets	Sensitivity/ PPA	Specificity/ NPA	TP	FN	TN	FP
BCID-GP	*Bacillus cereus* group	100.00%	100.00%	1	0	58	0
	Corynebacterium	100.00%	100.00%	1	0	58	0
	Enterococcus	100.00%	100.00%	6	0	53	0
	Enterococcus faecalis	100.00%	100.00%	4	0	55	0
	Enterococcus faecium	100.00%	100.00%	2	0	57	0
	Staphylococcus[1]	96.43%	100.00%	27	1	32	0
	Staphylococcus aureus	100.00%	100.00%	14	0	45	0
	Staphylococcus epidermidis[1]	90.91%	100.00%	10	1	49	0
	Staphylococcus lugdunensis	100.00%	100.00%	1	0	58	0
	Streptococcus	100.00%	100.00%	22	0	37	0
	Streptococcus agalactiae	100.00%	100.00%	3	0	56	0
	Streptococcus anginosus group	100.00%	100.00%	4	0	55	0
	Streptococcus pneumoniae	100.00%	100.00%	4	0	55	0
	Streptococcus pyogenes	100.00%	100.00%	2	0	57	0
	Pan Gram-Negative	100.00%	100.00%	4	0	55	0
	mecA[2]	100.00%	100.00%	7	0	52	0
BCID-GN	*Bacteroides fragilis*	100.00%	100.00%	4	0	40	0
	Citrobacter	100.00%	100.00%	1	0	43	0
	Enterobacter cloacae complex	100.00%	100.00%	3	0	41	0
	Escherichia coli	100.00%	100.00%	17	0	27	0
	Fusobacterium nucleatum	100.00%	100.00%	1	0	43	0
	Klebsiella pneumoniae	100.00%	94.74%	6	0	36	2
	Klebsiella oxytoca	100.00%	100.00%	3	0	41	0
	Morganella morganii[3]	100.00%	97.67%	1	0	42	1
	Pseudomonas aeruginosa	100.00%	100.00%	3	0	41	0
	Proteus	100.00%	100.00%	4	0	40	0
	Proteus mirabilis	100.00%	100.00%	3	0	41	0
	Salmonella	100.00%	100.00%	2	0	42	0
	Serratia marcescens	100.00%	97.73%	1	0	43	1
	Stenotrophomonas maltophilia	100.00%	100.00%	1	0	43	0
	CTX-M	100.00%	100.00%	6	0	38	0
	Pan Gram-Positive	100.00%	100.00%	3	0	41	0
BCID-FP	*C. albicans*	100.00%	100.00%	2	0	2	0

1) One CoNS identified in a co-infection by standard of care not detected on 1st ePlex BCID-GP tested, but *S. epidermidis* identified by ePlex BCID-GP on repeat
2) *mecA* only evaluated for *Staphylococcus aureus* in this study
3) *M. morganii* caused by resolved manufacturing issue in lot #, 1 additional *M. morganii* was detected during discordant testing from the same lot #

Conclusions

- ePlex BCID molecular panels significantly decrease turnaround time in the 107 samples tested creating opportunities to escalate and/or deescalate appropriate antibiotic use.
- In particular, 12% of patients tested were positive for either CTX-M, *vanA* or *mecA* resistance markers.
- On average, a 94.4% decrease in result turnaround time compared to our current methodology provides more timely information for appropriate change of treatment and isolation in 28% of patients tested in this study.
- Accurate identification of polymicrobial infections missed by standard of care, as well as the accurate identification of a *S. epidermidis* misreported as a *S. lugdunensis* provides invaluable information for appropriate treatment and patient safety.
- In conclusion, these panels will not only provide better management for patients with bloodstream infections, it will allow for a much more timely opportunity to treat with appropriate antibiotics, as well as, to implement our facilities Infection Control guidelines and isolation procedures.