



Head-to-Head Comparison of GenMarkDx ePlex and Luminex (Nanosphere) Gram Negative and Gram Positive Blood Culture Identification (BCID) Panels with Culture for Quality Improvement



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Up Dated Abstract

Background: Both GenMarkDx and Luminex have molecular diagnostic panels that can provide rapid diagnostic results for positive blood cultures. This study compares the performance of each system with each other and with culture.

Methods: Positive blood cultures were evaluated in real time Gram stains were performed to guide the choice of Gram Positive (GP) or Gram negative (GN) GenMarkDx ePlex (**BCID Panels for Research Use Only**) and Luminex **Verigene** BCID panel use. All testing followed the manufacturer's method. Culture and susceptibility results served as the gold standard. The data were categorized for concordance between the 2 systems. All results were defined as true or false positives and negatives (TP, FP, FN, TN) compared to culture, as "analyte not in panel" (ANIP) or "Probable Positives" (PP) where full identification and susceptibility were not performed, but results agreed between the systems.

Results: A total of 37 specimens were tested using the GN panel, 32 mono- and 5 polymicrobial. **Twenty-one (57%)** were concordant. The ePlex GN panels produced **44 TP, 1 FP, 3 FN and 4 ANIP** results. The **Verigene** panel produced 26 TP, 0 FP, 5 FN and **15 ANIP** results. Most discrepancies reflected ANIP result that were not detected by **Verigene**, but which were detected by the ePlex (3 *S. marcescens*, 3 *S. maltophilia*, 1 *M. morgani*, 1 *F. necrophorum*, and 2 Pan GP) as well as 2 ePlex panels that failed internal control. Discordant and FN results for both systems were seen in polymicrobial cultures.

For the GP panels, 74 specimens were tested, 59 mono- and 15 polymicrobial. **Excluding failed runs, 50/69 (72%)** were **completely** concordant. Discordant results were seen mostly in polymicrobial cultures and focused on coagulase negative Staphylococci. The ePlex GP produced **143 TP, 3 FP, 9 FN, 24 PP** and 3 ANIP results whereas the Nanosphere GP produced **120 TP, 0 FP, 9 FN, 24 PP**, and **13 ANIP** results. Five of the **FN** results represented *Staphylococcus* sp. when a definitive species had also been identified. Most of the ANIP results were redundant species designations. Overall, most discrepancies weren't substantial.

Conclusions: The ePlex GN panel demonstrated superior performance compared to Nanosphere due to the wider breadth of analytes available. In contrast, the GP panels both performed well with most discrepancies representing inconsequential differences. Both systems and both GP and GN panels had difficulties with polymicrobial cultures.

* Updates in red

Background

GenMark Diagnostics has developed the ePlex®, rapid comprehensive blood culture panels with detection capabilities similar to, but broader than the Luminex Verigene BCID panels.

- The two instruments use molecular diagnostics though they vary:
- The Luminex Verigene BCID system utilizes Microarray DNA capture for the detection of multiple target organism and resistance mechanisms in 1.5-2.5 hours of blood culture positivity
- The ePlex® consists of multiplex PCR using electrowetting technology followed by the detection of signal probe-DNA hybrid that is captured on a microarray target for specific eSensor™ detection of organisms and resistance genes in about 1.5 hours of culture positivity

Both systems provide rapid diagnostic blood culture results that can be delivered directly to a provider to optimize antimicrobial coverage for the patient. Both systems may play a critical role in antimicrobial stewardship. In this study, we evaluated the head-to-head performance of these 2 systems for validation and quality improvement.

Materials & Methods

Instrumentation:

- The ePlex® instrument serial number 1732100197 with 12 bays (A1-6 and B1-6) was utilized for this validation. Research use only (RUO) cartridge lot numbers 53064008 expiry 5/17/2019 & 53112746 expiry 7/20/2019 were used for this validation. Testing was rotated between bays (range 3-12 tests per bay).
- Verigene instrument Model 10-0000-02, serial number 12334140 with SP modules (A1-A4 and B1) was used for this validation. Various Lot numbers incorporated with the Utility kit and Nucleic acid test components were used to complete this validation, all of which were used within the expiration date limit.

Head-to-head testing patient specimens:

- Positive Blood Cultures (aerobic and anaerobic) were tested
- A total of 37 Gram negative patient specimens were tested by both systems
- A total of 74 Gram positive patient specimens were tested by both systems
- All specimens were confirmed using the lab's routine culture and susceptibility protocols:
 - Bruker MALDI-tof for most identifications
 - BD Phoenix for some identification and most susceptibility
 - Confirmation of some resistance mechanism occurred as required using E-test strip method

- The data were categorized for concordance between the 2 systems:
 - Results were defined as true or false positives and negatives (TP, FP, FN, TN) compared to culture
 - "analyte not in panel" (ANIP) was used if the panel did not detect the organism seen in culture
 - "Probable Positives" (PP) was used if full ID/susc. was not done, but ePlex and Verigene agreed

Table 1. Analyte Comparison for ePlex RUO and Verigene Gram Negative and Gram Positive Panels

GRAM POSITIVE PANEL		GRAM NEGATIVE PANEL	
ePlex	Verigene	ePlex	Verigene
Staphylococcus sp.	Staphylococcus sp.	Acinetobacter baumannii	Acinetobacter sp.
Staphylococcus aureus	Staphylococcus aureus	Bacteroides fragilis	
Staphylococcus epidermidis	Staphylococcus epidermidis	Citrobacter sp.	
Staphylococcus lugdunensis	Staphylococcus lugdunensis	Cronobacter sakazakii	
Streptococcus sp.	Streptococcus sp.	Enterobacter sp.	Enterobacter sp.
Streptococcus agalactiae	Streptococcus agalactiae	Enterobacter cloacae CIMPX	
Streptococcus anginosus	Streptococcus anginosus	Escherichia coli	Escherichia coli
Streptococcus pneumoniae	Streptococcus pneumoniae	Fusobacterium necrophorum	
Streptococcus pyogenes	Streptococcus pyogenes	Fusobacterium nucleatum	
Bacillus cereus group		Haemophilus influenzae	
Bacillus subtilis group		Klebsiella oxytoca	Klebsiella pneumoniae
Corynebacterium sp.		Klebsiella pneumoniae	
Cultibacterium acres		Morganiella morgani	
Lactobacillus sp.		Nisseria meningitidis	
Listeria sp.	Listeria sp.	Protosp. sp.	
Listeria monocytogenes		Protosp. mirabilis	
Enterococcus sp.		Pseudomonas aeruginosa	Pseudomonas aeruginosa
Enterococcus faecalis	Enterococcus faecalis	Salmonella sp.	
Enterococcus faecium	Enterococcus faecium	Serratia sp.	
Microroccus sp.		Serratia marcescens	
meCa		Stenotrophomonas maltophilia	
meCc		CTX-M	CTX-M
VAN A, VAN B	VAN A, VAN B	IMP, KPC, NDM, OXA, VIM	IMP, KPC, NDM, OXA, VIM
Pan Gram Negative		Pan Gram Positive	
Pan Candida		Pan Candida	

Results

Data for all tests producing a valid result by both ePlex and Verigene are listed in **Table 2** for the Gram Positives and **Table 3** for the Gram Negatives.

Failed Runs: There were 5 failed runs for ePlex GP panel and 2 for the ePlex GN panel which occurred early in the validation and resulted in a rebalancing of the instrument, which ended the failed runs. These runs produced no valid results. The data for the Verigene failed runs were inadvertently not tabulated. For this reason, the failed runs have not been included in any of the statistics.

Repeat Testing: Some, but not all significant discrepant results were repeated on the ePlex panels. When this occurred, both results are included in the ePlex statistics, but the Verigene results are listed only once since these assay were not repeated. In all 3 instances, repeat testing produced the correct and valid results.

Table 2: Overall Performance Characteristics of the ePlex and Verigene Gram Positive Panels Compared to Culture:

Acc #	Bottle Type	GS Morph.	Culture & Susceptibility Result	Single/Multi orgs	ePlex result	Verigene result	ePlex agree with Verig	ePlex agree with culture?	ePlex Result Classification	Verigene classification
H34159	R	GPCCLS	BSCN2(contaminant)	S	Staph. sp., S. epi.	S. epi.	NO	YES	PP S. epi. TP Staph. sp.	PP S. epi. FN Staph. sp.
M36887	R	GPCCLS	BSCN (contaminant)	S	Staph. sp.	Staph. sp.	YES	YES	TP Staph. sp.	TP Staph. sp.
W80234	R	GPCCLS	BSCN (contaminant)	S	Staph. sp.	Staph. sp.	YES	YES	TP Staph. sp.	TP Staph. sp.
W78238	R	GPCCLS	BSCN (contaminant)	S	Staph. sp.	Staph. sp.	YES	YES	TP Staph. sp.	TP Staph. sp.
H51991	R	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	PP S. epi., PP mecA TP Staph. sp.	PP S. epi., PP mecA TP Staph. sp.
W72258	R	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	PP S. epi., PP mecA TP Staph. sp.	PP S. epi., PP mecA TP Staph. sp.
X68171	R	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	PP S. epi., PP mecA TP Staph. sp.	PP S. epi., PP mecA TP Staph. sp.
F57961	R	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	PP S. epi., PP mecA TP Staph. sp.	PP S. epi., PP mecA TP Staph. sp.
X74836	R	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	PP S. epi., PP mecA TP Staph. sp.	PP S. epi., PP mecA TP Staph. sp.
M16923	N	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	PP S. epi., PP mecA TP Staph. sp.	PP S. epi., PP mecA TP Staph. sp.
M27939	R	GPCCLS	BT172-SCN, no GN (contaminant)	M	GN		NO	YES	FP PAN GN	PP S. epi., UNCONFIRMED Mech. TP Staph. sp., UNCONFIRMED Mech. TP Staph. sp.
T81996	N	GPCCLS	BSCN (contaminant)	S	Neg for all analytes	Staph. sp., S. epi., mecA	NO	NO	FN Staph. sp., (isolate was a contaminant)	UNCONFIRMED Mech. TP Staph. sp.
W13618	R	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	PP S. epi., PP mecA TP Staph. sp.	PP S. epi., PP mecA TP Staph. sp.
T81798	R	GPCCLS	BSCN (contaminant)	S	GN		NO	NO	FP PAN GN (respiatory virus + E coli)	PP Staph. sp., PP mecA, TP Staph. sp
W78238	R	GPCCLS	BSCN (contaminant)	S	Neg for all analytes	Staph. sp.	NO	NO	FN Staph. sp. (correctly Dled on rpt)	duplicate data
T72423	N	GNR	CI, perfringens, E. faecium, K. pneumoniae (2 sets)	M	Enterococcus sp., E. faecium	E. faecium	NO	NO	TP Enterococcus sp, TP E. faecium, FN Pan GN, Clostridium ANIP	TP E. faecium, Enterococcus sp. ANIP, Clostridium sp. ANIP
X79994	R	GPCCH	E. faecalis	S	Enterococcus sp., E. faecalis	E. faecalis	NO	YES	TP Enterococcus sp., TP E. faecalis	TP E. faecalis, Enterococcus sp. ANIP
T66116	R	GPCPCH	E. faecalis	S	Enterococcus sp., E. faecalis	E. faecalis	NO	YES	TP Enterococcus sp., TP E. faecalis	TP E. faecalis, Enterococcus sp. ANIP
W76044	R	GPCPH	E. faecalis	S	Enterococcus sp., E. faecalis	E. faecalis	NO	YES	TP Enterococcus sp., TP E. faecalis	TP E. faecalis, Enterococcus sp. ANIP
W57711	R	GPCPH	E. faecalis (vanc S)	S	Enterococcus sp., E. faecalis	E. faecalis	NO	YES	TP Enterococcus sp., TP E. faecalis	TP E. faecalis, Enterococcus sp. ANIP
S36780	N	GPCCLS	MRSA, E. faecium, VAN A	M	Enterococcus sp., S. aureus, meca	E. faecium, VAN A, Staph. sp., S. aureus, meca	NO	YES	TP Enterococcus sp., TP E. faecium, TP Staph. sp., TP S. aureus, TP meca, TP VAN A	TP E. faecium, TP VAN A, Enterococcus sp. ANIP
T70916	N	GPCCH	S. parvastrangiis	S	Strept. sp., S. agalactiae	Strept. sp.	YES	YES	TP Strept. sp.	TP Strept. sp.
M40827	N	GPCPRCHS	S. agalactiae	S	Strept. sp., S. agalactiae	Strept. sp., S. agalactiae	YES	YES	TP Strept. sp., TP S. agalactiae	TP Strept. sp., TP S. agalactiae
T60458	N	GPCCLS	S. aureus	S	Staph. sp., S. aureus	Staph. sp., S. aureus	YES	YES	TP Staph. sp., TP S. aureus	TP Staph. sp., TP S. aureus
N39443	N	GPCCLS	S. aureus	S	Staph. sp., S. aureus	Staph. sp., S. aureus	NO	YES	FN Staph. sp., TP S. aureus	FN Staph. sp., TP S. aureus
M33700	R	GPCCLS	S. aureus, MRSA	S	Staph. sp., S. aureus	Staph. sp., S. aureus	YES	YES	TP Staph. sp., TP S. aureus	TP Staph. sp., TP S. aureus
S54134	R	GPCCLS	MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
M18950	R	GPCCLS	S. aureus, MSSA	S	Staph. sp., S. aureus	Staph. sp., S. aureus	NO	YES	TP Staph. sp., TP S. aureus	TP S. aureus, FN Staph. sp.
W68321	N	GPCCLS	BSCN (contaminant)	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	TP Staph. sp., PP meca, PP S. epi.	TP Staph. sp., PP meca, PP S. epi.
W70198	R	GPCCLS	Staph. epi., OxR	S	Staph. sp., S. epi., mecA	Staph. sp., S. epi., mecA	YES	YES	TP Staph. sp., TP Staph. epi., TP meca	TP Staph. sp., TP Staph. epi., TP meca
X77294	R	GPCCL	hominis, ox R 2 sets	M	GN		NO	NO	S. epi.	TP Staph. sp., FN meca, PAN GN ANIP
X68074	R	GPCCLS	S. epi., S. hominis	M	Staph. sp., S. epi., meca	Staph. sp., S. epi., meca	YES	YES	TP Staph. sp., TP Staph. epi., TP meca	TP S. epi., TP Staph. sp., TP meca
M36596	R	GPCCLS	Staph. epi.-Cefoxitin R, OXR	M	Staph. sp., S. epi., meca	Staph. sp., S. epi., meca	YES	YES	TP Staph. sp., TP Staph. epi., TP meca	TP Staph. sp., TP Staph. epi., TP meca
W18215	R	GPCCLS	S. aureus, S. epi., meca	S	Staph. sp., S. aureus, S. epi., meca	Staph. sp., S. aureus, S. epi., meca	YES	YES	TP Staph. sp., TP meca, TP Staph. sp.	TP Staph. sp., TP meca, TP Staph. sp.
H33004	R	GPCCLS	meCA	M	S. aureus, S. epi.	S. aureus, S. epi.	NO	YES	FN meca (MECA detected on N bottle)	FN meca (MECA detected on N bottle)
X71767	R	GPCCLS	MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
W17219	R	GPCCLS	MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
T74517	N	GPCCLS	S. aureus, MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
T73915	R	GPCCLS	S. aureus, MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
X80834	N	GPCCLS	S. aureus, MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
W58492	R	GPCCLS	S. aureus, MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
S53881	R	GPCCLS	MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
W15020	R	GPCCLS	S. aureus	S	Staph. sp., S. aureus	Staph. sp., S. aureus	YES	YES	TP Staph. sp., TP S. aureus	TP Staph. sp., TP S. aureus
T54756	N	GPCCLS	S. aureus, MSSA	S	Staph. sp., S. aureus	Staph. sp., S. aureus	YES	YES	TP Staph. sp., TP S. aureus	TP Staph. sp., TP S. aureus
F60833	N	GPCCLS	S. aureus, MSSA	S	Staph. sp., S. aureus	Staph. sp., S. aureus	YES	YES	TP Staph. sp., TP S. aureus	TP Staph. sp., TP S. aureus
T64300	N	GPCCLS	S. aureus MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus, TP meca	TP Staph. sp., TP S. aureus, TP meca
H36077	R	GPCCLS	S. hominis, S. epi., meca (1 set drawn)	M	Staph. sp., meca	Staph. sp.	NO	YES	TP Staph. sp., TP meca, FN S. epi.	TP Staph. sp., FN S. epi., FN meca
W63245	R	GPCCLS	BSCN	S	Staph. sp.	Staph. sp.	YES	YES	TP Staph. sp.	TP Staph. sp.
F60180	R	GPC(R)	Cefoxitin R, OxR	M	Staph. sp., S. epi., meca	Staph. sp., S. epi., meca	YES	YES	TP Staph. sp., TP S. epi., TP meca	TP Staph. sp., TP S. epi., TP meca
T83305	N	GPR	probable Lysinibacillus fusiformis	S	Neg for all analytes		YES	NO	ANIP	ANIP
M28897	N	GPCCH	S. agalactiae	S	Strept. sp., S. agalactiae	Strept. sp., S. agalactiae	YES	YES	TP strep. sp., TP S. agalactiae	TP strep. sp., TP S. agalactiae
S53684	N	GPCCH	S. agalactiae	S	Strept. sp., S. agalactiae	Strept. sp., S. agalactiae	YES	YES	TP Strept. sp., TP S. agalactiae	TP Strept. sp., TP S. agalactiae
T83618	R	GPCPRCH	probable Strept. sp., probable Nisseria sp., Strept. anginosus	M	Strept. sp., S. anginosus, PAN GN	Strept. sp.	NO	YES	TP Strept. sp., TP S. anginosus, TP Pan GN	TP Strept. sp., S. anginosus not reported on this panel, PAN GN ANIP
W87561	N	GPCCLS	Cefoxitin R, S. epi. both sets	S	Neg for all analytes	Staph. sp., S. epi.	NO	NO	FN Staph. sp., FN S. epi.	TP Staph. sp., TP S. epi.
S36780	N	GPCCLS	MRSA, E. faecium, VAN A	M	Staph. sp., S. aureus, meca	E. faecium, VAN A, Staph. sp., S. aureus, meca	NO	NO	FN Enterococcus sp., FN E. faecium, FN VAN A (all analytes correctly Dled on rpt)	duplicate data
F81988	R	GPCCLS	MSSA	S	Staph. sp., S. aureus	Staph. sp., S. aureus	YES	YES	TP Staph. sp., TP S. aureus	TP Staph. sp., TP S. aureus
F85604	N	GPCPCH	S. pyogenes	S	Strept. sp., S. pyogenes	Strept. sp., S. pyogenes	YES	YES	TP Strept. sp., TP S. pyogenes	TP Strept. sp., TP S. pyogenes
H59268	R	GPCCLS	MRSA	S	Staph. sp., S. aureus, meca	Staph. sp., S. aureus, meca	YES	YES	TP Staph. sp., TP S. aureus	TP Staph. sp., TP S. aureus
M52224	N	GPCCH	Strept dysgalactiae	S	Strept. sp.,	Strept. sp.,	YES	YES	TP Strept. sp.	TP Strept. sp.
M55567	N	GPCPCH	Vanco R E. faecium	S	Enterococcus sp., E. faecium, VAN A	E. faecium, VAN A	NO	YES	TP Enterococcus sp., TP E. faecium, TP VAN A	TP E. faecium, TP VAN A, Enterococcus sp. ANIP
W81398	R	GPCCLS	BSCN	S	Staph. sp., S. epi., meca	Staph. sp., S. epi., meca	YES	YES	PP S. epi., PP meca, TP Staph. sp	