

# Performance of a Novel System for Rapid Identification and Susceptibility Testing Directly from Positive Pediatric Blood Cultures



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## Objective

- To evaluate the accuracy of the Accelerate Pheno™ system and PhenoTest™ BC kit (AXDX) for identification (ID) and antimicrobial susceptibility testing (AST) of blood pathogens in the pediatric population compared to standard of care (SOC) methods.

## Methods

**SOC Methods.** Blood culture bottles were incubated using the BACTEC™ automated blood culture system (BD Diagnostics, Sparks, MD). Microorganism ID from positive blood cultures was performed using the Bruker MALDI Biotyper Molecular Identification System (Bruker Daltonics, Billerica, MA) and biochemical testing when appropriate. AST was performed using the Microscan WalkAway-96 Plus system (Beckman Coulter, Brea, CA) and the Gram-positive PM29 and Gram-negative NM43 panels. AST interpretation was done using the Clinical Laboratory Standards Institute 2016 M100 criteria.

**Accelerate.** Positive blood culture broth from routine clinical care was used for testing on the Accelerate Pheno™ system following the manufacturer's instructions. The resulting data was analyzed using the pre-FDA clearance Accelerate Pheno™ system software (v1.0) producing ID results within 90 minutes and AST results within 7 hours.

**Discrepancy Testing.** Microorganism ID was performed using the Vitek®2 (BioMerieux, Durham, NC). AST was performed using broth-micro dilution testing performed in triplicate to determine the modal minimum inhibitory concentration. Cefoxitin disk diffusion testing was performed for methicillin resistance determination.

## Summary of Testing

**299 Accelerate runs performed**

- CHOA, n=150
- CMCD, n=149

**Runs Included, n=254 (85%)**

Determined by SOC testing:

- Monomicrobial, n=217
- Polymicrobial, n=37

**Runs Excluded, n=45 (15%):**

- >8 hr after culture positivity, n=6
- SOC failures/exclusions, n=2
- Accelerate technical failure, n=1

**Accelerate ID failures, n=36 (n=37 Organisms):**

**Missed on-panel organisms, n=8**

<i>C. albicans</i>	<i>S. capitis</i>
<i>S. epidermidis</i> (n=2)	<i>S. hominis</i> (n=2)
<i>S. mitis</i>	<i>S. pneumoniae</i>

**Off-panel organisms, n=29**

<i>Bifidobacterium</i> spp.	<i>B. cepacia</i>	<i>C. krusei</i>	<i>C. parapsilosis</i> (n=2)
<i>C. tropicalis</i> (n=2)	<i>Corynebacterium</i> spp. (n=2)	<i>E. meningoseptica</i>	<i>F. nucleatum</i>
<i>Granulicatella</i> spp.	<i>Haemophilus</i> spp. (n=3)	<i>Kocuria</i> spp.	<i>Lactobacillus</i> spp.
<i>Leuconostoc</i> spp.	<i>Micrococcus</i> spp. (n=2)	<i>Moraxella</i> spp. (n=3)	<i>R. mucilaginosus</i> (n=2)
<i>S. saprophyticus</i>	<i>S. anginosus</i>	<i>S. intermedius</i>	Viridans Group <i>Streptococcus</i> spp.

## Results

### Microorganism Targets and Antibiotics Tested by Accelerate Pheno™ system and PhenoTest™ BC kit

**Table 1.** List of Gram-positive bacteria, yeast and antibiotics evaluated by AXDX

Organism/Group	Ampicillin	Erythromycin	Trim/Sulfa	Daptomycin	Linezolid	Vancomycin	Cefoxitin (methicillin resistance)	ML-Sb (Ery-Clinda)
<i>Staphylococcus aureus</i>		X	X <sup>a</sup>	X	X	X	X	
<i>Staphylococcus lugdunensis</i>		X <sup>a</sup>	X <sup>a</sup>	X <sup>a</sup>	X <sup>a</sup>	X	X	X
CNS spp. <sup>b</sup>		X <sup>a</sup>		X	X <sup>a</sup>	X	X	X
<i>Enterococcus faecalis</i>	X			X	X	X		
<i>Enterococcus faecium</i>	X			X	X	X		
<i>Streptococcus</i> spp. <sup>c</sup>								
<i>Candida albicans</i>								
<i>Candida glabrata</i>								

<sup>a</sup> Research use only; <sup>b</sup> CNS spp. includes *S. epidermidis*, *S. haemolyticus*, *S. hominis*, *S. capitis*, and *S. warneri*; <sup>c</sup> *Streptococcus* spp. includes *S. mitis*, *S. oralis*, *S. galloyticus*, *S. agalactiae*, and *S. pneumoniae*.

**Table 2.** List of Gram-negative bacteria and antibiotics evaluated by AXDX

Organism/Group	Amp-Sul	Pip-Tazo	Cefazolin	Ceftazidime	Ceftriaxone	Cefepime	Ertapenem	Meropenem	Aztreonam	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin
<i>Escherichia coli</i>	X	X	X <sup>a</sup>	X	X	X	X	X	X	X	X	X	X
<i>Klebsiella</i> spp. <sup>b</sup>	X	X	X <sup>a</sup>	X	X	X	X	X	X	X	X	X	X
<i>Proteus</i> spp. <sup>c</sup>	X	X		X	X	X	X	X	X	X	X	X	X
<i>Serratia marcescens</i>		X		X	X	X	X	X	X	X	X	X	X
<i>Enterobacter</i> spp. <sup>d</sup>		X		X	X	X	X	X	X	X	X	X	X
<i>Citrobacter</i> spp. <sup>e</sup>		X		X	X	X	X	X	X	X	X	X	X
<i>Pseudomonas aeruginosa</i>		X		X		X	X		X	X	X	X	X
<i>Acinetobacter baumannii</i>		X								X			

<sup>a</sup> Research use only; <sup>b</sup> *Klebsiella* spp. includes *K. pneumoniae* and *K. oxytoca*; <sup>c</sup> *Proteus* spp. includes *P. mirabilis* and *P. vulgaris*; <sup>d</sup> *Enterobacter* spp. includes *E. aerogenes* and *E. cloacae*; <sup>e</sup> *Citrobacter* spp. includes *C. freundii* and *C. koseri*.

### Identification of Microorganisms From Blood Culture

**Table 3.** Correlation of microorganisms identified by AXDX and SOC

Organism	Matched Identifications	Discrepant Results
<b>Overall</b>	<b>216</b>	<b>47</b>
<b>Gram-positive Bacteria</b>	<b>147</b>	<b>31</b>
<i>S. aureus</i>	33	10
<i>S. lugdunensis</i>	0	1
CNS spp.	82	7
<i>Streptococcus</i> spp.	21	9
<i>E. faecalis</i>	9	2
<i>E. faecium</i>	2	2
<b>Gram-negative Bacteria</b>	<b>69</b>	<b>9</b>
<i>E. coli</i>	28	1
<i>Klebsiella</i> spp.	24	0
<i>S. marcescens</i>	2	1
<i>Proteus</i> spp.	1	0
<i>Citrobacter</i> spp.	3	1
<i>Enterobacter</i> spp.	9	1
<i>P. aeruginosa</i>	2	3
<i>A. baumannii</i>	0	2
<b>Yeast</b>	<b>0</b>	<b>7</b>
<i>C. albicans</i>	0	1
<i>C. glabrata</i>	0	6

**Table 4.** Discrepant results between AXDX and SOC

Discrepant Results	n	Discrepancy Resolution		Comments
		Gram Stain <sup>a</sup>	Same Genus	
<b>False Positive Organisms</b>	<b>34</b>	<b>13</b>	<b>10</b>	
<i>S. aureus</i>	9	2	–	
CNS spp.	3	3	–	
<i>Streptococcus</i> spp.	9	–	8	AXDX identified off panel targets <i>S. dysgalactiae</i> , <i>S. pyogenes</i> (x4), <i>S. anginosus</i> , <i>S. parvaquinosus</i> (x2), and <i>Rothia</i> sp. as <i>Streptococcus</i> spp.
<i>E. faecium</i>	2	–	1	AXDX identified off panel target <i>E. gallinarium</i> as <i>E. faecium</i>
<i>E. coli</i>	1	1	–	
<i>S. marcescens</i>	1	–	–	
<i>Citrobacter</i> spp.	1	–	–	Identified from polymicrobial blood culture
<i>A. baumannii</i>	1	–	1	AXDX identified off panel target <i>Acinetobacter nosocomialis</i> as <i>A. baumannii</i>
<i>C. albicans</i>	1	1	–	
<i>C. glabrata</i>	6	6	–	
<b>False Negative Organisms</b>	<b>7</b>	<b>1</b>	<b>0</b>	
<i>S. aureus</i>	1	–	–	Identified from polymicrobial blood culture
CNS spp.	2	–	–	One isolate identified from polymicrobial blood culture
<i>E. faecalis</i>	2	–	–	Both isolates identified from polymicrobial blood culture
<i>E. aerogenes</i>	1	–	–	
<i>P. aeruginosa</i>	1	–	–	Identified from polymicrobial blood culture
<b>Unresolved/Testing in Progress</b>	<b>8</b>	<b>–</b>	<b>–</b>	

<sup>a</sup> Discrepant results that could be mitigated by lack of Gram stain/organism correlation (i.e. GPC, GNR, or yeast).

### Antimicrobial Susceptibility Testing

**Table 5.** Results of individual antibiotic susceptibility testing for Gram-positive bacteria

Antibiotic	n	Essential Agreement n (%)	Categorical Agreement n (%)	Very Major Errors	Major Errors	Minor Errors
<b>Gram-positive Bacterial Susceptibility Testing</b>	<b>486</b>	<b>473 (97.3)</b>	<b>476 (97.9)</b>	<b>3</b>	<b>1</b>	<b>6</b>
Ampicillin	11	11 (100)	11 (100)	0	0	0
Daptomycin	115	112 (97.4)	114 (99.1)	0	1	0
Erythromycin	104	99 (95.2)	96 (92.3)	3	0	5
Linezolid	115	115 (100)	115 (100)	0	0	0
Trimethoprim-Sulfamethoxazole	26	26 (100)	26 (100)	0	0	0
Vancomycin	115	110 (95.7)	114 (99.1)	0	0	1

**Table 6.** Results of antibiotic susceptibility testing for Gram-negative bacteria

Antibiotic	n	Essential Agreement n (%)	Categorical Agreement n (%)	Very Major Errors	Major Errors	Minor Errors
<b>Gram-negative Bacterial Susceptibility Testing</b>	<b>733</b>	<b>701 (95.6)</b>	<b>679 (92.6)</b>	<b>4</b>	<b>5</b>	<b>45</b>
Amikacin	59	59 (100)	59 (100)	0	0	0
Ampicillin-Sulbactam	45	43 (95.6)	34 (75.6)	0	2	9
Aztreonam	57	56 (98.2)	56 (98.2)	0	0	1
Cefazolin	40	39 (97.5)	33 (82.5)	0	0	7
Cefepime	59	57 (96.6)	54 (91.5)	0	0	5
Ceftazidime	60	47 (78.3)	46 (76.7)	0	1	13
Ceftriaxone	58	55 (94.8)	55 (94.8)	3	0	0
Ciprofloxacin	60	60 (100)	59 (98.3)	0	0	1
Ertapenem	57	57 (100)	57 (100)	0	0	0
Gentamicin	59	57 (96.6)	58 (98.3)	0	0	1
Meropenem	60	58 (96.7)	56 (93.3)	0	2	2
Piperacillin-Tazobactam	59	54 (91.5)	53 (89.8)	0	0	6
Tobramycin	60	59 (98.3)	59 (98.3)	1	0	0

## Results

### Methicillin and MLSb Antimicrobial Resistance Testing

**Table 7.** Antimicrobial susceptibility testing for β-lactam and inducible clindamycin resistance for *S. aureus* and CNS spp.

Cefoxitin and MLSb Testing for Antimicrobial Resistance	n	Categorical Agreement n (%)
<i>S. aureus</i> , methicillin-susceptible	8	8 (100)
<i>S. aureus</i> , methicillin-resistance	18	18 (100)
CNS spp., methicillin-susceptible	36	33 (91.7)
CNS spp., methicillin-resistance	37	35 (94.6)
CNS spp., MLSb positive	21	20 (95.2)
CNS spp., MLSb negative	30	29 (96.7)

### Off Target Organisms

**Table 8.** Organisms identified by SOC methods but not targets on the AXDX (valid runs).

Microorganisms	n
Total	47
Viridans Group <i>Streptococcus</i> spp.	8
<i>Streptococcus pyogenes</i>	5
<i>Bacillus</i> spp.	5
<i>Candida lusitanae</i>	2
<i>Candida tropicalis</i>	2
<i>Corynebacterium</i> spp.	4
<i>Haemophilus influenzae</i>	3
<i>Rothia</i> spp.	3
<i>Stenotrophomonas maltophilia</i>	3
<i>Salmonella typhi</i>	2
<i>Staphylococcus</i> spp.	2
<i>Acinetobacter nosocomialis</i>	1
<i>Burkholderia cepacia</i>	1
<i>Dermabacter hominis</i>	1
<i>Elizabethkingia meningoseptica</i>	1
<i>Enterococcus gallinarum</i>	1
<i>Micrococcus luteus</i>	1
<i>Neisseria flavescens</i>	1
<i>Streptococcus dysgalactiae</i>	1

## Conclusions

- The Accelerate Pheno™ system and PhenoTest™ BC kit correctly identified ~83% of Gram-positive and Gram-negative microorganisms recovered from blood cultures by SOC methods.
  - Overall ID sensitivity of 96.0% and specificity of 99.1%
- The majority of false positive ID results were due to off panel targets that were phylogenetically related to targets on the AXDX.
- The majority of false negative ID results were observed in polymicrobial blood cultures.
- Antibiotic susceptibility testing resulted in an overall essential agreement of 96.2% and categorical agreement of 94.8%. Compared to SOC testing, AXDX had 7 very major errors (S→R), 6 major errors (R→S), and 51 minor errors.
- FDA approved software v1.2 improves erythromycin AST results and correct ID of *Enterobacter* spp. and *Pseudomonas aeruginosa*.
  - AXDX FDA cleared testing requires Gram stain correlation to mitigate the reporting of false positive organism identifications.

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