A Multisite Clinical Evaluation of the LifeScale AST System for Rapid Antimicrobial Susceptibility Testing of Less Prevalent Gram-Negative Bacteria Direct from Blood Culture

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HEALTH-SUN-221
Sunday 06/07/2026

Abstract

Background:
Rapid antimicrobial susceptibility testing (rAST) is essential for guiding effective therapy and limiting antimicrobial resistance. Beyond common pathogens, less prevalent organisms, such as E. cloacae complex and C. freundii, also pose clinical challenges in bloodstream infections, emphasizing the need for rapid and accurate susceptibility testing to guide appropriate therapy.

The LifeScale AST system, developed by Affinity Biosensors (Santa Barbara, CA), is a multiplexed in vitro diagnostic test that utilizes a microfluidic sensor and resonant frequency to calculate organism concentration and mass distribution for quantitative AST. A multisite clinical evaluation was conducted to assess the substantial equivalence of the LifeScale System's LSGN Panel for less prevalent Gram-negative organisms compared to the CLSI reference broth microdilution method (BMD).

Methods:
The objective of the study was to establish clinical performance of the LifeScale AST system when compared to the CLSI BMD for determining quantitative (MIC) AST results directly from less prevalent Gram-negative positive blood cultures, including *E. cloacae complex*, *Citrobacter spp.*, *M. morganii*, *P. mirabilis*, *P. vulgaris*, *Providencia spp.*, *Salmonella spp.*, and *S. marcescens*.

Acceptable clinical performance for seeded clinical and challenge strains was assessed across the following parameters for *12 antimicrobial agents on the LSGN panel: essential agreement (EA), categorical agreement (CA), and the number and percent of categorical errors (minor, major, and very major errors). EA was calculated as the percentage of MIC results that fell within ±1 doubling dilution of the reference result. CA was calculated as the percentage of the LifeScale interpretive results (S/SDD/I/R) that were identical to the interpretive categories of the BMD result.

Results:
The LifeScale AST system demonstrated high agreement rates with the CLSI BMD for less prevalent Enterobacterales species, achieving overall essential agreement (EA) and categorical agreement (CA) rates of 96.4% and 97.6%, respectively. Error rates were within FDA-acceptable limits, with consistent performance observed across the less prevalent species and all antimicrobials.

Conclusion:
The LifeScale AST system offers faster, more accurate, and scalable testing compared to conventional methods. Strong EA and CA agreement in studies with less prevalent organisms underscores its potential as a leading platform in rapid diagnostics and improved patient outcomes.

Introduction

Rapid antimicrobial susceptibility testing (AST) is critical for timely management of bloodstream infections and optimization of antimicrobial therapy. Bloodstream infections caused by Gram-negative organisms are associated with significant morbidity and mortality, particularly in hospitalized and critically ill patients.

While diagnostic development has largely focused on common pathogens, less prevalent Enterobacterales, including *Enterobacter cloacae complex*, *Citrobacter freundii*, and *Proteus mirabilis*, remain clinically important due to variable resistance mechanisms, including AmpC β-lactamase production.

Conventional methods are time-consuming and may delay targeted therapy. The LifeScale AST system is a rapid, microfluidics-based platform designed to provide phenotypic results directly from positive blood cultures.

Methods

A multisite clinical evaluation was performed to assess the performance of the LifeScale AST system (LSGN panel) for less prevalent Gram-negative organisms recovered directly from positive blood cultures.

Antimicrobials Evaluated
The study evaluated 12 of the 14 antimicrobial agents on the LSGN panel, Table 1.

Table 1. Antimicrobials evaluated

Antimicrobial		Range µg/mL	
		Min	Max
Ampicillin	AMP	2	64
Aztreonam	AZT	1	64
Cefepime	FEP	0.5	64
Ceftazidime	TAZ	1	64
Ceftazidime-Avibactam	CZA	2	32
Ertapenem	ERT	0.125	8
Gentamicin	GEN	1	32
Levofloxacin	LEVO	0.25	16
Meropenem	MERO	0.125	16
Meropenem-Vaborbactam	MEV	0.5	16
Piperacillin-Tazobactam	P/T	4	256
Trimethoprim-Sulfamethoxazole	SXT	0.25	8

Organisms Evaluated:
The study included the following Gram-negative organisms:
Enterobacter cloacae complex, Citrobacter spp. (Citrobacter freundii, Citrobacter koseri), Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia spp. (Providencia rettgeri, Providencia stuartiii), Salmonella spp., and *Serratia marcescens.*

Table 2. Number of samples tested.

Sample Type	Total No. Samples Tested
Contemporary Samples	260
Stock Samples	106
Challenge Samples	86
Total Tested	**432**

Comparator Method:
Performance of the LifeScale system was compared to the reference method using CLSI broth microdilution (BMD). Testing was conducted at 3 sites with a diverse less prevalent strain set including seeded blood culture and challenge strains.

Performance Metrics:

- System performance was assessed using the following metrics:
- Essential Agreement (EA): MIC within ±1 doubling dilution of BMD
- Categorical Agreement (CA): concordance of susceptibility categories (S, I/SDD, R)
- Error rates: minor error, major error, and very major error classifications per FDA criteria

LifeScale AST Workflow and Technology:
Positive blood culture bottles were processed directly without subculture. A defined aliquot of positive blood culture broth was prepared and inoculated into the LifeScale LSGN AST panel, which contains pre-dispensed antimicrobial concentrations, Figure 1.

Panels were placed into the LifeScale instrument, where the system performs fully automated workflow steps including inoculation, incubation, measurement, and analysis. The instrument uses microfluidic sensor technology to monitor growth dynamics at the single-cell level, measuring changes in microbial mass and replication over time.

Following a short incubation period, the system generates high-resolution population growth profiles for each antimicrobial condition, Figure 2. These data are analyzed using automated computational algorithms and population-based modeling to determine minimum inhibitory concentrations (MICs).

Final MIC values are interpreted using FDA/CLSI breakpoints, and results are reported as categorical interpretations (Susceptible, Intermediate/Susceptible Dose Dependent, or Resistant) with full automation and minimal hands-on time.

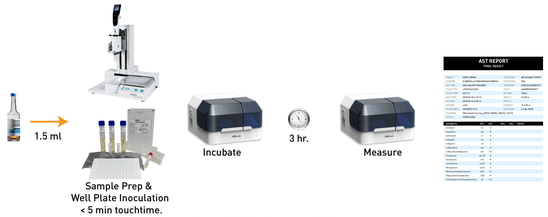

Figure 1. LifeScale workflow.

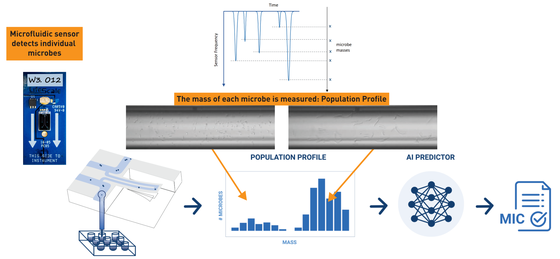

Figure 2. LifeScale core technology

Population profiles are generated for all antibiotics and antibiotic concentrations on the LifeScale panel. LifeScale's powerful Artificial Intelligence Predictor (AI-Predictor) analyzes this rich dataset to produce the correct MIC, even in cases where analyzing growth alone is insufficient, Figure 3.

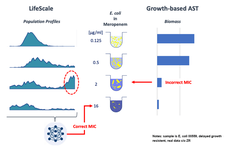

Figure 3. Standard growth-based AST

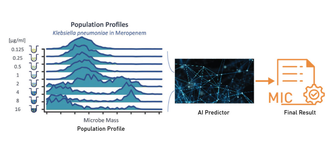

Figure 4. AI processing of population profile data

By combining the population profile data with advanced AI, LifeScale can determine correct MICs even for delayed-growth phenotypes, Figure 4. The key is the information contained in individual cell masses. Delayed-growth strains may not replicate for several hours; however, during LifeScale's short incubation time, microbes still respond to antibiotics by changing their morphology and mass producing filamentous forms or spheroplasts. LifeScale's population profiles clearly reveal these responses, whereas a growth-based AST can miss them, since they occur prior to replication and visible biomass increase.

Results

The LifeScale AST system demonstrated strong agreement with BMD across less prevalent Gram-negative organisms.

- **Essential Agreement (EA): 96.4%**
- **Categorical Agreement (CA): 97.6%**
- **Error rates: All within FDA acceptance criteria**

Performance was consistent across all evaluated organisms and antimicrobial agents on the LSGN panel.

These results support the LifeScale AST system as a robust and accurate method for rapid MIC based susceptibility testing directly from positive blood culture with less prevalent organisms.

Table 3. LifeScale LSGN Essential Agreement Performance: Interpretation of MIC Results is based on FDA Susceptibility Test Criteria and the CLSI M100

Organism	% Essential Agreement										
	Antimicrobials Tested										
	AMP	AZT	FEP	TAZ	CZA	ETP	GEN	LEVO	MERO	MEV	P/T	SXT
Citrobacter freundii		95.5%	90.0%	90.0%	95.2%	90.2%	100.0%	97.7%	95.5%	93.2%		
Citrobacter koseri		98.5%		94.1%	100.0%	98.5%	100.0%	98.5%	94.1%	97.1%	94.1%	100.0%
Enterobacter cloacae complex		97.6%	100.0%	90.7%	100.0%	92.7%	100.0%	94.0%	92.7%	95.2%		
Morganella morganii		95.1%	92.5%	95.1%	100.0%	97.4%		97.6%		95.0%		
Proteus mirabilis	98.2%	92.7%	100.0%	98.2%	96.3%			90.9%	90.9%	94.5%	98.2%	100.0%
Proteus vulgaris		89.3%	100.0%	100.0%				96.6%			96.6%	96.4%
Providencia rettgeri		95.2%	100.0%		100.0%	100.0%		100.0%		100.0%	95.5%	
Providencia stuartii		100.0%	100.0%	92.9%	100.0%	100.0%		100.0%		100.0%	100.0%	
Serratia marcescens		98.1%	94.3%	94.3%	98.1%	90.2%	98.1%	100.0%	98.1%	100.0%	94.3%	
Salmonella spp.	100.0%											

Table 4. LifeScale LSGN Categorical Agreement Performance: Interpretation of MIC Results is based on FDA Susceptibility Test Criteria and the CLSI M100

Organism	% Categorical Agreement										
	Antimicrobials Tested										
	AMP	AZT	FEP	TAZ	CZA	ETP	GEN	LEVO	MERO	MEV	P/T	SXT
Citrobacter freundii		100.0%	95.5%	100.0%	100.0%	95.1%	97.7%	88.6%	97.7%	97.7%		
Citrobacter koseri		100.0%		97.1%	100.0%	98.5%	98.5%	97.1%	98.5%	97.1%	91.2%	100.0%
Enterobacter cloacae complex		100.0%	97.6%	97.7%	100.0%	90.2%	100.0%	90.0%	97.6%	97.6%		
Morganella morganii		100.0%	92.5%	95.1%	100.0%	97.4%		97.6%		100.0%		
Proteus mirabilis	100.0%	98.2%	100.0%	98.2%	100.0%			96.4%	98.2%	96.4%	98.2%	100.0%
Proteus vulgaris		100.0%	100.0%	100.0%				93.1%			96.6%	96.4%
Providencia rettgeri		100.0%	100.0%		100.0%	100.0%		88.9%		95.5%	95.5%	
Providencia stuartii		100.0%	100.0%	92.9%	100.0%	100.0%		100.0%		100.0%	93.3%	
Serratia marcescens		98.1%	100.0%	94.3%	100.0%	96.1%	96.2%	92.5%	100.0%	100.0%	94.3%	
Salmonella spp.	100.0%											

Table 5. LifeScale LSGN Overall Performance Summary for Less prevalent Organisms

Antibiotic	Total	EA (No.)	EA (%)	Eval EA	Eval EA (%)	CA (No.)	CA (%)	R	S	MIN (n,%)	MAJ (n,%)	VMJ (n,%)
Ampicillin – *P. mirabilis*	55	54	98.2%	2	50.0%	55	100%	15	40	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ampicillin – *Salmonella spp.*	20	20	100%	1	100%	20	100%	3	17	0 (100%)	0 (100%)	0 (100%)
Aztreonam	365	350	95.9%	42	64.3%	363	99.5%	47	316	2 (0.55%)	0 (0.00%)	0 (0.00%)
Cefepime	299	289	96.7%	27	63.0%	293	98.0%	29	265	6 (2.01%)	0 (0.00%)	0 (0.00%)
Ceftazidime-Avibactam	337	332	98.5%	9	44.4%	337	100%	20	317	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ertapenem	278	263	94.6%	28	46.4%	268	96.4%	33	243	8 (2.88%)	2 (0.82%)	0 (0.00%)
Gentamicin	206	205	99.5%	10	90.0%	202	98.1%	22	182	4 (1.94%)	0 (0.00%)	0 (0.00%)
Levofloxacin	371	359	96.8%	79	84.8%	348	93.8%	73	284	22 (5.93%)	1 (0.35%)	0 (0.00%)
Meropenem	261	246	94.3%	23	34.8%	257	98.5%	25	234	4 (1.53%)	0 (0.00%)	0 (0.00%)
Meropenem-Vaborbactam	339	326	96.2%	17	23.5%	332	97.9%	17	319	7 (2.06%)	0 (0.00%)	0 (0.00%)
Piperacillin-Tazobactam	242	232	95.9%	26	61.5%	229	94.6%	20	220	10 (4.13%)	3 (1.36%)	0 (0.00%)
Trimethoprim-Sulfamethoxazole	165	163	98.8%	6	66.7%	164	99.4%	49	116	0 (0.00%)	0 (0.00%)	1 (2.04%)

Conclusions

By combining microfluidic technology with resonant frequency–based sensing, the LifeScale system delivers rapid, quantitative antimicrobial susceptibility testing results in approximately 4.5 hours, substantially reducing time to optimized therapy. This accelerated turnaround, along with strong EA/CA performance, supports its application across a broad range of organisms, including less prevalent Gram-negative species.

Overall, these findings support integration of the LifeScale AST system into clinical workflows, where earlier susceptibility reporting may facilitate more timely targeted therapy, enhance antimicrobial stewardship, and improve patient outcomes. Across all 3 study sites, the system demonstrated high levels of speed, accuracy, and reproducibility, reinforcing its utility for rapid AST in both common and less frequently encountered organisms.