



**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY**

I Background Information:

A 510(k) Number

K251875

B Applicant

Affinity Biosensors, LLC

C Proprietary and Established Names

LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SAN	Class II	21 CFR 866.1650 - A Cellular Analysis System For Multiplexed Antimicrobial Susceptibility	MI - Microbiology
LON	Class II	21 CFR 866.1645 - Fully automated short-term incubation cycle antimicrobial susceptibility system	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system, previously cleared in K211815 and K241324, to:

1. Expand the indications for use to include testing of additional Enterobacterales species with FDA STIC-recognized breakpoints.

2. Remove and/or update limitations for aztreonam, cefepime, ceftazidime, and ceftazidime-avibactam.
3. Re-analyze performance with current FDA STIC-recognized breakpoints for cefepime, ceftazidime and piperacillin-tazobactam with *Pseudomonas aeruginosa*.

B Measurand:

Antimicrobial		Range µg/mL	
		Min (≤)	Max (>)
Amikacin	AMI	4	256
Ampicillin	AMP	2	64
Aztreonam	AZT	1	64
Cefazolin	FAZ	0.25	16
Cefepime	FEP	0.5	64
Ceftazidime	TAZ	1	64
Ceftazidime-avibactam	CZA	2/4	32/4
Ertapenem	ETP	0.12	8
Gentamicin	GEN	1	32
Levofloxacin	LEVO	0.25	16
Meropenem	MERO	0.12	16
Meropenem-vaborbactam	MEV	0.5/8	16/8
Piperacillin-tazobactam	P/T	4/4	256/4
Trimethoprim-sulfamethoxazole	SXT	0.25	8

C Type of Test:

The LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system is a quantitative antimicrobial susceptibility test system that determines the minimum inhibitory concentration of specific organisms from positive blood culture samples.

III Intended Use/Indications for Use:

A Intended Use(s):

The LifeScale AST system is a multiplexed *in vitro* diagnostic test that uses a microfluidic sensor and resonant frequency to calculate organism concentration and/or mass distribution for quantitative antimicrobial susceptibility testing (AST). Testing is performed directly on blood cultures signaled as positive by a continuous monitoring blood culture system and confirmed by Gram stain. The LifeScale AST system does not provide organism identification and is not indicated for use with polymicrobial samples. Interpretive results (Susceptible/Intermediate/Susceptible-dose dependent/Resistant) are provided for specific drug/organism combinations. Results are intended to be used in conjunction with other clinical and laboratory findings. Standard laboratory protocols for processing positive blood cultures should be followed to ensure availability of isolates for supplemental testing as needed. Additionally, subculture of positive blood culture is necessary for the susceptibility testing of organisms present in polymicrobial samples, for testing antimicrobial agents and species not

indicated for testing with the device and for epidemiologic testing and for recovery of organisms present in microbial samples.

B Indication(s) for Use:

Testing is indicated for *Acinetobacter* spp., Enterobacterales, *Pseudomonas aeruginosa*, and *Salmonella* spp. as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC). The LSGN Kit with LifeScale AST system has demonstrated acceptable performance with the following organisms :

- Amikacin: *Acinetobacter* spp. (*A. baumannii* complex, *A. calcoaceticus*, *A. lwoffii*, *A. pittii*, *A. radioresistens*, *A. ursingii*)
- Ampicillin: Enterobacterales (*Escherichia coli*, *Proteus mirabilis*), and *Salmonella* spp.
- Aztreonam: Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia rettgeri*, *Providencia stuartii*, *Serratia marcescens*), and *Pseudomonas aeruginosa*
- Cefazolin: Enterobacterales (*Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella variicola*)
- Cefepime: Enterobacterales (*Citrobacter freundii*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia rettgeri*, *Providencia stuartii*, *Serratia marcescens*), and *Pseudomonas aeruginosa*
- Ceftazidime: *Acinetobacter* spp. (*A. baumannii* complex, *A. calcoaceticus*, *A. lwoffii*, *A. pittii*, *A. radioresistens*), Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Klebsiella variicola*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia stuartii*, *Serratia marcescens*), and *Pseudomonas aeruginosa*
- Ceftazidime-avibactam: Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Proteus mirabilis*, *Providencia rettgeri*, *Providencia stuartii*, *Serratia marcescens*)
- Ertapenem: Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Providencia rettgeri*, *Providencia stuartii*, *Serratia marcescens*)
- Gentamicin: Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Klebsiella variicola*, *Serratia marcescens*)
- Levofloxacin: Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia rettgeri*, *Providencia stuartii*, *Serratia marcescens*), and *Pseudomonas aeruginosa*

- Meropenem: *Acinetobacter* spp. (*A. baumannii* complex, *A. calcoaceticus*, *A. lwoffii*, *A. pittii*, *A. radioresistens*, *A. ursingii*), Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Serratia marcescens*), and *Pseudomonas aeruginosa*
- Meropenem-vaborbactam: Enterobacterales (*Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Proteus mirabilis*, *Providencia rettgeri*, *Providencia stuartii*, *Serratia marcescens*)
- Piperacillin-tazobactam: *Acinetobacter* spp. (*A. baumannii* complex), Enterobacterales (*Citrobacter koseri*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia rettgeri*, *Providencia stuartii*, *Serratia marcescens*), and *Pseudomonas aeruginosa*,
- Trimethoprim-sulfamethoxazole: Enterobacterales (*Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella variicola*, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*)

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Limitations

1. Perform an alternative method of testing prior to reporting results for the following antimicrobial/organism combination(s):
 - Cefazolin: *P. mirabilis*
 - Ceftazidime: *Pr. rettgeri*
 - Ertapenem: *P. mirabilis*, *P. vulgaris*
 - Gentamicin: *P. mirabilis*, *P. vulgaris*
 - Meropenem: *M. morganii*, *P. vulgaris*
 - Piperacillin-tazobactam: *M. morganii*
2. Perform an alternative method of testing prior to reporting results for:
 - Ertapenem: *Enterobacter cloacae* complex at MIC value of 2 µg/mL due to the occurrence of one major error (1/29 susceptible isolates, 3.5%)
 - Piperacillin-tazobactam: *Proteus vulgaris* at MIC value of 32 µg/mL due to the occurrence of one major error (1/28) susceptible isolates, (3.6%)
 - Cefepime: *Pseudomonas aeruginosa* at MIC 4µg/mL due to the occurrence of one very major error (1/21 resistant isolates, 4.7%).
3. The LifeScale Gram Negative Kit (LSGN) showed unacceptable performance for:
 - *E. coli* with Meropenem-vaborbactam when tested using the following blood culture bottle types: bioMérieux FA Plus Aerobic, bioMérieux FN Plus Anaerobic, and BD BACTEC Plus Anaerobic. Use alternate bottle types for determining Meropenem-vaborbactam MICs for *E. coli*.

- *A. baumannii* with Amikacin when tested using the following blood culture bottle types: bioMérieux Standard Aerobic, FA Plus Aerobic, and VersaTREK REDOX 1 Aerobic. Use alternate bottle types for determining Amikacin MICs for *A. baumannii*.
4. The performance of the LifeScale Gram Negative Kit (LSGN) panel has been evaluated using the following blood culture bottles:
 - BD BACTEC: Standard Aerobic, Standard Anaerobic, Plus Aerobic, Plus Anaerobic, Lytic Anaerobic
 - BacT/ALERT: Standard Aerobic, Standard Anaerobic, FA Plus Aerobic, FN Plus Anaerobic
 - VersaTREK: REDOX 1 Aerobic media, REDOX 2 Anaerobic media
 5. The ability of the LifeScale Gram Negative Kit (LSGN) to detect resistance in the following antimicrobial/organism combinations is unknown because of an insufficient number of resistant isolates were available during the clinical study:
 - Ceftazidime-avibactam: *C. koseri*
 - Meropenem-vaborbactam: *C. koseri*, *M. morganii*

Refer to the device labeling for limitations described in K211815 and K241324 and a complete list of antimicrobial/organism indications and evaluated bottle types.

D Special Instrument Requirements:

The LifeScale Gram Negative Kit (LSGN) is performed on the LifeScale instrument with Software version 2.6.1805.

IV Device/System Characteristics:

A Device Description:

The device description for the LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system was previously described in K211815. Briefly, the LifeScale Gram Negative Kit (LSGN) and the LifeScale AST system is a semi-automated instrument system for antimicrobial susceptibility testing (AST) directly from positive blood cultures for which the Gram stain shows gram-negative bacilli. The system uses a microfluidic sensor that detects organisms in suspension and measures differences in cell mass between bacterial suspensions incubated in the presence and absence of antibiotic. Minimum inhibitory concentrations (MICs) are determined from data obtained during sample measurement including organism concentration and/or cell mass distributions of individual organisms. The system automatically interprets the measurements to determine MIC values and interpretive results (susceptible, susceptible dose dependent, intermediate, or resistant) based on FDA STIC-recognized breakpoints. The organism identification determined using a platform FDA-cleared for use with positive blood culture samples is entered by the user. If the organism identification has not been entered or if the sample has not been confirmed as monomicrobial, the system provides a preliminary report that indicates that organism identification or monomicrobial status is pending. The device Instructions for Use indicates that the preliminary laboratory report should not be reported to the healthcare provider. The final report is provided to the healthcare provider when the organism identification is entered into the system and the culture is confirmed to be monomicrobial.

Polymicrobial samples should not be tested with the LifeScale Gram Negative Kit (LSGN). Preliminary results are available in most cases within four hours from initiation of the assay.

Refer to the [K211815](#) Decision Summary for additional details.

Table 1 provides the reportable MIC ranges and breakpoints for antimicrobial agents claimed for testing with the LifeScale Gram Negative Kit (LSGN).

Table 1. Reportable MIC Ranges and Species-Specific Breakpoints for Antimicrobials Included in the LifeScale Gram Negative Kit (LSGN)

Antimicrobial	Tested Species	LifeScale Reportable Range (µg/mL)	FDA-Recognized Breakpoints			
			S	SDD	I	R
Ampicillin	Enterobacterales	≤2 - >64	≤8		16	≥32
	<i>Salmonella</i> spp.					
Aztreonam	Enterobacterales	≤1 - >64	≤4		8	≥16
	<i>Pseudomonas aeruginosa</i>		≤8		16	≥32
Cefazolin	Enterobacterales	≤0.25 - >16	≤2		4	≥8
Ceftazidime	<i>Acinetobacter</i> spp.	≤1 - >64	≤8		16	≥32
	Enterobacterales		≤4		8	≥16
	<i>Pseudomonas aeruginosa</i>		≤8		16	≥32
Ertapenem	Enterobacterales	≤0.125 - >8	≤0.5		1	≥2
Trimethoprim-Sulfamethoxazole	Enterobacterales	≤0.25 - >8	≤2/38		-*	≥4/76
Amikacin	<i>Acinetobacter</i> spp.	≤4 - >256	≤16		32	≥64
Cefepime	Enterobacterales	≤0.5 - >64	≤2	4-8	-*	≥16
	<i>P. aeruginosa</i>		≤8		16	≥32
Ceftazidime-avibactam	Enterobacterales	≤2/4 - >32/4	≤8/4		-*	≥16/4
Gentamicin	Enterobacterales	≤1 - >32	≤2		4	≥8
Levofloxacin	Enterobacterales	≤0.25 - >16	≤0.5		1	≥2
	<i>Pseudomonas aeruginosa</i>		≤1		2	≥4
Meropenem	<i>Acinetobacter</i> spp.	≤0.12 - >16	≤2		4	≥8
	Enterobacterales		≤1		2	≥4
	<i>Pseudomonas aeruginosa</i>		≤2		4	≥8
Meropenem-vaborbactam	Enterobacterales	≤0.5 - >16	≤4/8		8/8	≥16/8
Piperacillin-tazobactam	<i>Acinetobacter</i> spp.	≤4 - >256	≤16/4		32/4-64/4	≥128/4
	Enterobacterales		≤8/4		16/4	≥32/4
	<i>Pseudomonas aeruginosa</i>		≤16/4		32/4	≥64/4

S = Susceptible; SDD = Susceptible-dose dependent; I = Intermediate; R = Resistant

*No intermediate category is defined for these drug/organism combinations. For some drug organism combinations, the SDD is defined instead of an intermediate category.

B Principle of Operation:

The principles of operation for the LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system are previously described in K211815. Briefly, the LifeScale AST system uses a microfluidic sensor with a vibrating microchannel to detect and measure the mass of individual microorganisms in culture samples. As microbes flow through the sensor, each organism causes a frequency dip proportional to its mass, allowing the system to count organisms and measure their individual masses along with fluid volume. The MIC Analysis software processes this data to determine minimum inhibitory concentrations (MICs) for antibiotics, and the same measurement method is used to prepare sample inoculum by diluting organism suspensions to target concentrations.

Refer to the [K211815](#) Decision Summary for additional details.

Quality Control:

Quality control (QC) is performed by the operator using manufacturer-specified organisms (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 700603, and *Enterobacter cloacae* ABGNQC1) appropriate for each antimicrobial agent. The QC AST reports “out of range” for any MIC results that are not consistent with expected MIC QC ranges.

V Substantial Equivalence Information:

A Predicate Device Name(s):

LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system

B Predicate 510(k) Number(s):

K241324

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K251875</u> (New Device)	<u>K241324</u> (Predicate Device)
Device Trade Name	LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system	Same
General Device Characteristic Similarities		
Intended Use/Indications For Use	The LifeScale AST system is a multiplexed <i>in vitro</i> diagnostic test that uses a microfluidic sensor and resonant frequency to calculate organism concentration and/or mass distribution for quantitative antimicrobial susceptibility testing (AST). Testing is performed directly on blood cultures signaled as positive by a continuous monitoring blood culture system and confirmed by Gram stain. The LifeScale AST	Same

Device & Predicate Device(s):	<u>K251875</u> (New Device)	<u>K241324</u> (Predicate Device)
	<p>system does not provide organism identification and is not indicated for use with polymicrobial samples. Interpretive results (Susceptible/Susceptible-dose dependent/Intermediate/Resistant) are provided for specific drug/organism combinations. Results are intended to be used in conjunction with other clinical and laboratory findings. Standard laboratory protocols for processing positive blood cultures should be followed to ensure availability of isolates for supplemental testing as needed. Additionally, subculture of positive blood culture is necessary for the susceptibility testing of organisms present in polymicrobial samples, for testing antimicrobial agents and species not indicated for testing with the device, for epidemiologic testing and for recovery of organisms present in microbial samples.</p> <p>The LifeScale Gram Negative Kit (LSGN) is intended for use with the LifeScale AST system for <i>in vitro</i> testing of positive blood culture samples confirmed by Gram stain as containing gram-negative bacilli.</p>	
Sample	Blood cultures signaled as positive by a continuous monitoring blood culture system.	Same
Inoculation Method	Automated	Same
Read Method	Automated	Same
Result Report	Report results as a minimum inhibitory concentration (MIC) and categorical interpretation (S, I/SDD, R)	Same
Sample Preparation	Centrifugation and pipetting of sample	Same
IVD Functions	AST	Same
Instrument	LifeScale AST system	Same

Device & Predicate Device(s):	<u>K251875</u> (New Device)	<u>K241324</u> (Predicate Device)
Technology	Microfluidic and resonant frequency to calculate organism concentration and/or mass distribution	Same
Antimicrobial Agents	Amikacin Cefepime Ceftazidime-avibactam Gentamicin Levofloxacin Meropenem Meropenem-vaborbactam Piperacillin-tazobactam Ampicillin Aztreonam Cefazolin Ceftazidime Ertapenem Trimethoprim-sulfamethoxazole	Same
Breakpoint Change Protocol (PCCP)	Describes planned modifications to update breakpoints when FDA STIC-recognized breakpoints are updated, as published on the FDA STIC website. Incorporated by reference K211815 and K241324.	Same
General Device Characteristic Differences		
Organisms Tested	<i>Acinetobacter</i> spp. (<i>Acinetobacter baumannii</i> complex, <i>Acinetobacter baumannii/nosocomialis</i> group, <i>A. calcoaceticus</i> , <i>A. lwoffii</i> , <i>A. pittii</i> , <i>A. radioresistens</i> , <i>A. ursingii</i>) Enterobacterales (<i>Citrobacter freundii</i> , <i>Citrobacter koseri</i> , <i>Enterobacter cloacae</i> complex, <i>Escherichia coli</i> , <i>Klebsiella aerogenes</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella pneumoniae</i> , <i>Klebsiella variicola</i> , <i>Morganella morganii</i> , <i>Proteus mirabilis</i> , <i>Proteus vulgaris</i> , <i>Providencia rettgeri</i> , <i>Providencia stuartii</i> , <i>Serratia marcescens</i>) <i>Pseudomonas aeruginosa</i>	<i>Acinetobacter</i> spp. (<i>Acinetobacter baumannii</i> complex, <i>Acinetobacter baumannii/nosocomialis</i> group, <i>A. calcoaceticus</i> , <i>A. lwoffii</i> , <i>A. pittii</i> , <i>A. radioresistens</i> , <i>A. ursingii</i>) Enterobacterales (<i>Escherichia coli</i> , <i>Klebsiella aerogenes</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella pneumoniae</i> , <i>Klebsiella variicola</i>)

Device & Predicate Device(s):	<u>K251875</u> (New Device)	<u>K241324</u> (Predicate Device)
	<i>Salmonella</i> spp.	<i>Pseudomonas aeruginosa</i>

VI Standards/Guidance Documents Referenced:

- FDA Class II Special Controls Guidance Document: Antimicrobial Susceptibility (AST) Systems; Guidance for Industry and FDA (Issued August 28, 2009).
- CLSI M100-Ed 35, *Performance Standards for Antimicrobial Susceptibility Testing*; 2025.
- CLSI M07. 11th ed. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 2018.
- CLSI M07. 12th ed. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 2024.
- FDA STIC Website FDA-Recognized Antimicrobial Susceptibility Test Interpretive Criteria
- IEC 60601-1-2 Edition 4.1 2020-09 CONSOLIDATED VERSION, Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance
- IEC 61010-1 Edition 3.1 2017-01, Safety requirements for electrical equipment for measurement, control, and laboratory use
- IEC 62304 Edition 1.1 2015-06 Consolidated Version, Medical device software - Software life cycle processes

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The reproducibility of the LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system was previously assessed in K211815 and K241324. This submission does not include the addition of new antimicrobials or new organism reporting groups; therefore, the previous reproducibility testing is acceptable. Refer to the [K211815](#) and [K241324](#) Decision Summaries for additional details.

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

The potential impact of interfering substances on the results of the LifeScale Gram Negative Kit (LSGN) LifeScale with the AST system was previously assessed in K211815 and K241324. Refer to the [K211815](#) and [K241324](#) Decision Summaries for additional details.

4. Media Equivalency Study:

A media equivalency study was conducted to assess compatibility of the LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system with various commonly used blood culture bottle types. Three blood culture bottle types from two different blood culture manufacturers [bioMérieux, Inc. (BacT/Alert: FA Plus Aerobic, FN Plus Anaerobic) and Becton Dickinson (BACTEC: Plus Anaerobic)] were evaluated analytically with the LifeScale Gram Negative Kit (LSGN). A total of 14 well-characterized isolates (strains) of *E. coli*, *K. pneumoniae*, *A. baumannii* and *P. aeruginosa* were inoculated into each blood culture bottle type; ten replicates of each resulting positive blood culture were tested using the LifeScale Gram Negative Kit (LSGN) within 12 hours of positivity. BD BACTEC bottles were incubated in a continuous monitoring blood culture instrument; BacT/Alert bottle types were incubated in a conventional incubator with or without mixing per the bottle instructions for use. The time to positivity for the BacT/Alert blood culture bottles was estimated based on color change indicator at the bottom of the bottle and confirmed by LifeScale AST system cell counts.

In addition, for aztreonam/*P. aeruginosa*, four additional blood culture bottle types from three different manufacturers [bioMérieux, Inc. (BacT/Alert: Standard Aerobic), Becton Dickinson (BACTEC: Standard Aerobic and Plus Aerobic), and ThermoFisher (VersaTREK: REDOX 1 Aerobic media)] were evaluated. Two well characterized strains of *P. aeruginosa* were inoculated into each blood culture bottle type; ten replicates of each resulting positive blood culture were tested using the LifeScale Gram Negative Kit (LSGN). BACTEC bottles were incubated in a continuous monitoring blood culture instrument; other bottle types were incubated in a conventional incubator with or without mixing per the bottle instructions for use. The time to positivity was estimated for the BacT/Alert and VersaTREK blood culture bottles based on time to positivity for BACTEC media and confirmed by LifeScale AST system cell counts.

In the original 510(k) pre-market submission (K211815), the MIC results for each bottle type with each antimicrobial/organism combination were compared to the mode MIC value obtained with the broth microdilution reference method. However, the current 510(k) pre-market submission follows a different comparison approach. The approach is similar to the approach used in K241324 where the individual results from the new bottle types were directly compared to the LifeScale AST system mode MIC for the BD BACTEC Standard Aerobic (i.e., the “comparator”) directly. The acceptance criteria of EA \geq 95% for each antimicrobial/bottle type was applied to this direct comparison approach.

Results for most drug/organism combinations for tested species showed acceptable performance with all blood culture bottles with the following exceptions, which were mitigated with limitations outlined below for each case:

- Results obtained with the combination of amikacin/*A. baumannii* with bioMérieux FA Plus Aerobic showed low EA when compared to the comparator, BD BACTEC Standard Aerobic Media.

To address the results obtained with amikacin/*A. baumannii* the following limitation was included in the device labeling:

The LifeScale Gram Negative Kit (LSGN) showed unacceptable performance for A. baumannii with Amikacin when tested using the following blood culture bottle types: bioMérieux FA Plus Aerobic. Use alternative bottle types for determining Amikacin MICs for A. baumannii.

- Results obtained with the combination of meropenem-vaborbactam/*E. coli* with bioMérieux FA Plus Aerobic, bioMérieux FN Plus Anaerobic, and BD BACTEC Plus Anaerobic showed low EA when compared to the comparator, BD BACTEC Standard Aerobic Media.

To address the results obtained with meropenem-vaborbactam/*E. coli* the following limitation was included in the device labeling:

The LifeScale Gram Negative Kit (LSGN) kit showed unacceptable performance for E. coli with Meropenem-vaborbactam when tested using the following blood culture bottle types: bioMérieux FA Plus Aerobic, bioMérieux FN Plus Anaerobic, and BD BACTEC Plus Anaerobic. Use alternative bottle types for determining Meropenem-vaborbactam MICs for E. coli.

5. Assay Reportable Range:

Not applicable.

6. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Sample Stability, Off-line and On-line Incubation, and Cross Contamination/Carry-Over were previously assessed in K211815 and K241324. Refer to the [K211815](#) and [K241324](#) Decision Summaries for additional details.

Quality Control Testing

Quality control testing was performed each day that testing was conducted during the clinical and analytical studies. Quality control samples were prepared from isolated colonies as described in the LifeScale Gram Negative kit (LSGN) Instructions for Use. Briefly, a 0.5 McFarland suspension of Gram-negative, CLSI-recommended, quality control strains were used to inoculate the LifeScale Gram Negative Kit (LSGN) and the reference broth microdilution method. The LifeScale AST system will measure the inoculum concentration and calculate the dilution required to inoculate the LifeScale Gram Negative Kit (LSGN). At least one QC organism was tested each day of the clinical and study testing with all QC organisms being tested weekly per clinical study site.

For all antimicrobials, except for gentamicin and meropenem, greater than 95% of LifeScale Gram Negative Kit (LSGN) results obtained during the clinical study were within the expected range; quality control results were acceptable (Table 2 below). For gentamicin and meropenem, the LifeScale Gram Negative Kit (LSGN) QC results were not within the expected range likely due to frequency of subculturing, which may have caused decline in

viability and strain integrity. All out of range QC results were repeated with fresh subculture and were within expected range and were considered acceptable.

Table 2. QC Results for the LifeScale Gram Negative Kit (LSGN), Clinical Study

Antimicrobial	QC Strain	Expected Range µg/mL	No. in Range/No. Tested (%)	
			Reference	LifeScale
Amikacin	<i>E. cloacae</i> ABGNQC1 ^a	8 - 32	28/28 (100)	79/80 (98.8)
Ampicillin	<i>E. coli</i> ATCC 25922 ^b	2-8	29/29 (100)	82/82 (100)
Aztreonam	<i>P. aeruginosa</i> ATCC 27853	2-8	34/36 (94.4) ^c	82/83 (98.8)
Cefazolin	<i>E. coli</i> ATCC 25922	1-4	29/29 (100)	82/82 (100)
Cefepime	<i>P. aeruginosa</i> ATCC 27853 ^b	≤0.5 - 4	36/36 (100)	81/81 (100)
Ceftazidime	<i>K. pneumoniae</i> ATCC 700603	16-64	30/30 (100)	77/77 (100)
Ceftazidime-avibactam	<i>E. cloacae</i> ABGNQC1 ^a	≤2/4 - 8/4	28/28 (100)	79/80 (98.8)
Ertapenem	<i>P. aeruginosa</i> ATCC 27853	2-8	33/36 (91.6) ^c	83/83 (100)
Gentamicin	<i>E. cloacae</i> ABGNQC1 ^a	8 - 32	26/28 (92.9) ^c	75/80 (93.8) ^c
Levofloxacin	<i>P. aeruginosa</i> ATCC 27853	0.5 - 4	33/36 (91.6) ^c	81/81 (100)
Meropenem	<i>P. aeruginosa</i> ATCC 27853 ^b	≤0.12 - 1	36/36 (100)	72/81 (88.9) ^c
Meropenem-vaborbactam	<i>E. cloacae</i> ABGNQC1 ^a	4/8 - 16/8	28/28 (100)	80/80 (100)
Piperacillin-tazobactam	<i>K. pneumoniae</i> ATCC 700603	8/4 - 32/4	30/30 (100)	77/77 (100)
Trimethoprim-sulfamethoxazole	<i>E. coli</i> ATCC 25922 ^b	≤0.5/9.5	29/29 (100)	82/82 (100)

^a Validation performed for non-CLSI recommended QC strain described in [K241324](#).

^b Does not include full CLSI expected range. Results were considered acceptable.

^c All out of range QC results were repeated with fresh subculture and were within expected range. Results are considered acceptable.

Inoculum Density Check: Organism concentration is determined automatically by the instrument. The ability of the LifeScale AST system to appropriately prepare inoculum was previously described in K211815 and K241324. Refer to the [K211815](#) and [K241324](#) Decision Summaries for additional information.

LifeScale Gram Negative Kit (LSGN) Tests Initiated and Failed to Report a Result.

Overall, 5.63% of tests initiated during the analytical and clinical studies failed to provide a result (Table 3).

Table 3. LifeScale Gram Negative Kit (LSGN) Tests Initiated and Failed to Report a Result

Reason for Exclusion/Incomplete Test	No. Exclusion or Incomplete Test/Total No. of Tests (%)		
	Clinical Study	QC	Overall
Plate Failures^a	0/432 (0.0)	0/332 (0.0)	0/764 (0.0)
Growth Failures	0/432 (0.0)	2/332 (0.6)	2/764 (0.3)
LifeScale Failures^b	6/432 (1.4)	3/332 (0.9)	9/764 (1.2)
Other Reasons^c	29/432 (6.7)	3/332 (0.9)	32/764 (4.2)
Total Excluded/Incomplete Tests	35/432 (8.1)	8/332 (2.4)	43/764 (5.6)

^a Plate failures include: unable to verify positive controls, sensor clog detected, system unable to calculate MIC.

^b LifeScale failures include: LifeScale system software and hardware failures

^c Other Reasons include: operator error, incubation time greater than 8 hours, user canceled, protocol error

Purity Check: Purity checks were performed for all clinical and analytical tests. Testing was not performed on samples with mixed growth or contamination.

7. Detection Limit:

Not applicable

8. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

Clinical performance testing with the LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system was conducted using contrived blood culture samples. Testing isolates were prepared by Affinity Biosensors and shipped frozen to three clinical study sites. Additionally, the three clinical sites tested contemporary/stock isolates, representative of their clinical center, that were pre-approved by Affinity Biosensors. The antimicrobials cleared in K211815 and K241324 were tested with additional organisms including *Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia rettgeri*, *Providencia stuartii*, *Salmonella* spp. and *Serratia marcescens*. As clinical prevalence of these species in clinical blood cultures was low and performance was previously established for the organism reporting group, testing with contrived samples was considered acceptable

Blood culture bottles containing the required blood volume were spiked with isolated, pure organisms and incubated on the corresponding blood culture system. Once flagged positive,

positive blood cultures were tested on the LifeScale AST system using the LifeScale Gram Negative Kit (LSGN) per the manufacturer's instructions for use. Subcultures were performed to confirm purity. In total, 432 positive blood cultures were tested across all sites: 240 contemporary isolates, 106 stock isolates, and 86 challenge isolates, including resistant isolates and isolates with on-scale MIC results.

AST testing was performed using the reference broth microdilution (BMD) method, as described in the CLSI document *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*, M07, 11th and 12th editions. Reference BMD panels were run in triplicate for each isolate and an MIC mode was determined for comparison with the LifeScale Gram Negative Kit (LSGN) MIC result. If an MIC mode could not be established from the first three BMD results, a second set of BMD assays was run in triplicate and the MIC mode across all six tests was determined. If a mode still could not be established, the median MIC was used for comparison with the LifeScale Gram Negative Kit (LSGN) MIC result.

LifeScale Gram Negative Kit (LSGN) with the LifeScale AST System performance was based on criteria outlined in the *Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems*. Performance criteria included essential agreement (EA) and 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 LifeScale Gram Negative Kit (LSGN) interpretive results (S/I/SDD/R) that were identical to the interpretive categories of the reference result. For drug/organism group combinations in this submission where the susceptible-dose dependent category is recognized in place of the intermediate category (S/SDD/R), any errors that were observed with this category were designated as minor errors.

Positive blood culture samples containing more than one organism should not be tested with the LifeScale AST system. The following limitations are included in the device labeling:

Testing with the LifeScale AST system should not be performed on polymicrobial samples.

If the subculture (purity) plate indicates the sample is polymicrobial, the AST results should be voided, and susceptibility testing on each isolate using an alternative method with standard inoculum preparation should be performed.

A summary of the performance of LifeScale Gram Negative Kit (LSGN) is described below for each antimicrobial agent with indicated species. Complete details including EA, CA and error rate analysis per organism group are summarized in Table 4.

Amikacin/Enterobacterales. A total of 115 Enterobacterales samples [*C. freundii* (44), *E. cloacae* complex (42), *P. vulgaris* (29)] were evaluated with amikacin with the aim to expand testing with additional Enterobacterales species beyond what was cleared in K241324. With the current FDA STIC-recognized breakpoints for amikacin (≤ 4 (S), 8 (I), ≥ 16 (R)), the susceptible breakpoint is now the lowest dilution of the LifeScale Gram Negative Kit (LSGN) reporting range, ≤ 4 - >256 . As a result, this device does not meet the device design requirements outlined in the AST Special Control Guidance because it does not report one

dilution below the Susceptible breakpoint. A complete evaluation of performance could not be conducted for this device to determine substantial equivalence for this antimicrobial/organism group combination. Therefore, this indication was not cleared, and the device labeling has been updated accordingly to remove any claims or limitations related to amikacin/Enterobacterales.

Ampicillin/Enterobacterales. A total of 55 Enterobacterales samples [*P. mirabilis* (55)] were evaluated with ampicillin. Testing demonstrated an EA of 98.2% and CA of 100%, which is acceptable. There were no minor, major, or very major errors.

Ampicillin/Salmonella spp. A total of 20 *Salmonella* spp. samples were evaluated with ampicillin. Testing demonstrated an EA of 100% and a CA of 100%, which is acceptable. There were no minor, major, or very major errors.

Note: FDA STIC fully recognizes CLSI M100 35th edition with no exceptions for ampicillin, which includes a reporting group for *Salmonella* spp. separate from Enterobacterales. For ampicillin, *Salmonella* spp. breakpoints are identical to the breakpoints recognized for Enterobacterales; therefore, testing was considered acceptable.

Aztreonam/Enterobacterales. A total of 365 Enterobacterales samples [*C. freundii* (44), *C. koseri* (66), *E. cloacae* complex (42), *M. organii* (41), *P. mirabilis* (55), *P. vulgaris* (28), *Pr. rettgeri* (22), *Pr. stuartii* (14), *S. marcescens* (53)] were evaluated with aztreonam. Testing demonstrated an EA of 95.9% and CA of 99.5%, which is acceptable. There were two minor errors and no major or very major errors.

Cefazolin/Enterobacterales. A total of 55 Enterobacterales samples [*P. mirabilis* (55)] were evaluated with cefazolin. Testing demonstrated an EA of 92.7% and a CA of 58.2%. The CA is not acceptable despite the EA of evaluable results being 91.1%. In addition, there were 21 minor errors, two (11.8%, 2/17) major errors and no very major errors. Reporting limitations were not appropriate to mitigate the unacceptable high minor and major errors. Therefore, the following limitation is included in the device labeling:

Perform an alternative method of testing prior to reporting results for cefazolin/P. mirabilis.

Cefepime/Enterobacterales. A total of 299 Enterobacterales samples [*C. freundii* (44), *E. cloacae* complex (42), *M. organii* (40), *P. mirabilis* (55), *P. vulgaris* (28), *Pr. rettgeri* (22), *Pr. stuartii* (15), *S. marcescens* (53)] were evaluated with cefepime. Testing demonstrated an EA of 96.6% and CA of 98.0%, which is acceptable. There were six minor errors and no major or very major errors.

Ceftazidime/Enterobacterales. A total of 346 Enterobacterales samples [*C. freundii* (44), *C. koseri* (68), *E. cloacae* complex (43), *M. organii* (41), *P. mirabilis* (55), *P. vulgaris* (28), *Pr. stuartii* (14), *S. marcescens* (53)] were evaluated with ceftazidime. Testing demonstrated an EA of 94.4% and CA of 97.1%, which is acceptable. There were nine minor errors, no major errors and one very major error (1.85%, 1/54). When evaluating results by individual species, *M. organii* had one very major error (16.7%, 1/6). Due to the limited number of resistant isolates tested with this species, the error was considered random. To address this,

the following footnote is included in the *LifeScale LSGN Clinical Performance* table in the labeling:

*One very major error (VMJ) was observed with ceftazidime when testing *Morganella morganii* that resulted in an unacceptable VMJ rate (16.7%, 1/6). This was considered random due to the limited number of resistant *Morganella morganii* isolates tested.*

Ceftazidime-avibactam/Enterobacterales. A total of 337 Enterobacterales samples [*C. freundii* (42), *C. koseri* (67), *E. cloacae* complex (42), *M. morganii* (42), *P. mirabilis* (54), *Pr. rettgeri* (22), *Pr. stuartii* (15), *S. marcescens* (53)] were evaluated with ceftazidime-avibactam. Testing demonstrated an EA of 98.5% and CA of 100%, which is acceptable. There were no minor, major, or very major errors.

The following limitation statement is included in the device labeling to address the lack of testing with resistant *C. koseri*:

*The ability of the LifeScale Gram Negative Kit (LSGN) to detect resistance in the following antimicrobial/organism combinations is unknown because of an insufficient number of resistant isolates were available during the clinical study: Ceftazidime-avibactam: *C. koseri*.*

Ertapenem/Enterobacterales. A total of 278 Enterobacterales samples [*C. freundii* (41), *C. koseri* (68), *E. cloacae* complex (41), *M. morganii* (39), *Pr. rettgeri* (23), *Pr. stuartii* (15), *S. marcescens* (51)] were evaluated with ertapenem. Testing demonstrated an EA of 94.6% and CA of 96.4%, which is acceptable. There were eight minor, two (0.8%, 2/243) major, and no very major errors. When evaluating results by individual species, *E. cloacae* complex had one major error (3.45%, 1/29), which is not acceptable. To address this unacceptable very major error rate, the following limitation is included in the device labeling:

Perform an alternative method of testing prior to reporting results for:

- *Ertapenem: Enterobacter cloacae complex at MIC value of 2µg/mL due to the occurrence of one major error (1/29 susceptible isolates, 3.5%).*

Gentamicin/Enterobacterales. A total of 206 Enterobacterales samples [*C. freundii* (44), *C. koseri* (66), *E. cloacae* complex (43), *S. marcescens* (53)] were evaluated with gentamicin. Testing demonstrated an EA of 99.5% and CA of 98.1%, which is acceptable. There were four minor errors and no major, or very major errors. Additionally, using the current FDA STIC-recognized breakpoints, performance for previously cleared Enterobacterales were re-analyzed by the sponsor and labeling updates we made accordingly.

Levofloxacin/Enterobacterales. A total of 371 Enterobacterales samples [*C. freundii* (44), *C. koseri* (68), *E. cloacae* complex (50), *M. morganii* (41), *P. mirabilis* (55), *P. vulgaris* (29), *Pr. rettgeri* (18), *Pr. stuartii* (13), *S. marcescens* (53)] were evaluated with levofloxacin. Testing demonstrated an EA of 96.8% and CA of 93.8%, which is acceptable. There were 22 minor, one (0.4%, 1/283) major, and no very major errors.

Meropenem/Enterobacterales. A total of 261 Enterobacterales samples [*C. freundii* (44), *C. koseri* (68), *E. cloacae* complex (41), *P. mirabilis* (55), *S. marcescens* (53)] were evaluated with meropenem. Testing demonstrated an EA 94.3% and CA of 98.5%, which is acceptable. There were four minor errors and no major or very major errors.

Meropenem-vaborbactam/Enterobacterales. A total of 339 Enterobacterales samples [*C. freundii* (44), *C. koseri* (68), *E. cloacae* complex (42), *M. morganii* (40), *P. mirabilis* (55), *Pr. rettgeri* (22), *Pr. stuartii* (15), *S. marcescens* (53)] were evaluated with meropenem/vaborbactam. Testing demonstrated an EA of 96.2% and CA of 98.0%, which is acceptable. There were seven minor errors and no major or very major errors.

The following limitation statement is included in the device labeling to address the lack of testing with resistant *C. koseri* and *M. morganii*:

The ability of the LifeScale Gram Negative Kit (LSGN) to detect resistance in the following antimicrobial/organism combinations is unknown because of an insufficient number of resistant isolates were available during the clinical study: Meropenem-vaborbactam: C. koseri, M. morganii

Piperacillin-tazobactam/Enterobacterales. A total of 242 Enterobacterales samples [*C. koseri* (68), *P. mirabilis* (55), *P. vulgaris* (29), *Pr. rettgeri* (22), *Pr. stuartii* (15), *S. marcescens* (53)] were evaluated with piperacillin/tazobactam. Testing demonstrated an EA of 95.9% and CA of 94.6%, which is acceptable. There were ten minor, three (1.4%, 3/220) major, and no very major errors. When evaluating results by individual species, *P. vulgaris* demonstrated one major error (3.6%, 1/28). To address this unacceptable major error rate, the following limitation is included in the device labeling:

Perform an alternative method of testing prior to reporting results for:

- *Piperacillin/tazobactam: Proteus vulgaris at MIC value of 32µg/mL due to the occurrence of one major error (3.6%, 1/28).*

Trimethoprim-sulfamethoxazole/Enterobacterales. A total of 165 Enterobacterales samples [*E. cloacae* complex (43), *M. morganii* (40), *P. mirabilis* (54), *P. vulgaris* (28)] were evaluated with trimethoprim-sulfamethoxazole. Testing demonstrated an EA of 98.8% and CA of 99.4%, which is acceptable. There were no minor or major errors and one (2.0, 1/49) very major error. Due to the lack of an intermediate breakpoint, further analysis of the errors was performed, and adjustments were made by considering the MIC values of the errors compared to the reference MIC values. The one very major error is in essential agreement with the reference MIC values. Therefore, the very major error rate was adjusted to 0% (0/49).

Table 4. Performance for All Antimicrobial Agents with All Organisms Groups

	Tot	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
Ampicillin Enterobacterales[^]													

	Tot	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
[Breakpoints (µg/mL): ≤8 (S), 16 (I), ≥ 32(R)]													
Seeded Challenge	12	12	100	0	0	N/A	12	100	8	4	0	0	0
Seeded Clinical	43	42	97.7	2	1	50	43	100	7	36	0	0	0
Combined	55	54	98.2	2	1	50	55	100	15	40	0	0	0
Ampicillin Salmonella spp.^													
[Breakpoints (µg/mL): ≤8 (S), 16 (I), ≥ 32(R)]													
Seeded Clinical	20	20	100	1	1	100	20	100	3	17	0	0	0
Combined	20	20	100	1	1	100	20	100	3	17	0	0	0
Aztreonam Enterobacteriales^													
[Breakpoints (µg/mL): ≤4 (S), 8 (I), ≥16 (R)]													
Seeded Challenge	75	67	89.2	25	17	68.0	74	98.6	37	37	1	0	0
Seeded Clinical	290	283	97.6	17	10	58.8	289	99.7	10	279	1	0	0
Combined	365	350	95.9	42	27	64.3	363	99.5	47	316	2	0	0
Cefepime Enterobacteriales^													
[Breakpoints (µg/mL): ≤2 (S), 4,8 (SDD*), >16 (R)]													
Seeded Challenge	67	61	91.0	17	11	64.7	63	94.0	29	36	4	0	0
Seeded Clinical	232	228	98.3	10	6	60.0	230	99.1	0	229	2	0	0
Combined	299	289	96.7	27	17	63.0	293	98.0	29	265	6	0	0
Ceftazidime Enterobacteriales^#													
[Breakpoints (µg/mL): ≤4 (S), 8 (I), ≥16 (R)]													
Seeded Challenge	74	67	90.5	19	12	63.2	68	91.9	43	26	5	0	1
Seeded Clinical	272	260	95.6	18	6	33.3	268	98.5	11	260	4	0	0
Combined	346	327	94.5	37	18	48.7	336	97.1	54	286	9	0	1
Ceftazidime-avibactam Enterobacteriales^													
[Breakpoints (µg/mL): ≤8/4 (S), ≥16 (R)]													
Seeded Challenge	64	63	98.4	5	4	80.0	64	100	20	44	0	0	0
Seeded Clinical	273	269	98.5	4	0	0	273	100	0	273	0	0	0
Combined	337	332	98.5	9	4	44.4	337	100	20	317	0	0	0
Ertapenem Enterobacteriales^													
[Breakpoints (µg/mL): ≤0.5 (S), 1(I), ≥2.0 (R)]													
Seeded Challenge	54	52	96.3	8	6	75	53	98.2	30	23	1	0	0
Seeded Clinical	224	211	94.2	20	7	35	215	96.0	3	220	7	2	0
Combined	278	263	94.6	28	13	46.4	268	96.4	33	243	8	2	0

	Tot	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
Gentamicin Enterobacterales[^] [Breakpoints (µg/mL): ≤2 (S), 4 (I), ≥8 (R)]													
Seeded Challenge	40	40	100	5	5	100	38	95	20	19	2	0	0
Seeded Clinical	166	165	99.4	5	4	80	164	98.8	2	163	2	0	0
Combined	206	205	99.5	10	9	90	202	98.1	22	182	4	0	0
Levofloxacin Enterobacterales [Breakpoints (µg/mL): ≤0.5 (S), 1 (I), ≥2 (R)]													
Seeded Challenge	75	68	90.7	44	37	84.1	64	85.3	45	20	11	0	0
Seeded Clinical	295	290	98.3	35	30	85.7	283	95.9	28	263	11	1	0
Combined	370	358	96.8	79	67	84.8	347	93.8	73	283	22	1	0
Meropenem Enterobacterales[^] [Breakpoints (µg/mL): ≤1 (S), 2 (I), ≥4 (R)]													
Seeded Challenge	52	42	80.1	15	5	33.3	50	96.2	25	25	2	0	0
Seeded Clinical	209	204	97.6	8	3	37.5	207	99.0	0	209	2	0	0
Combined	261	246	94.3	23	8	34.8	257	98.5	25	234	4	0	0
Meropenem-vaborbactam Enterobacterales[^] [Breakpoints (µg/mL): ≤4/8 (S), 8/8 (I), ≥16/8 (R)]													
Seeded Challenge	65	54	83.1	15	4	26.7	58	89.2	17	45	7	0	0
Seeded Clinical	274	272	99.3	2	0	0	274	100	0	274	0	0	0
Combined	339	326	96.2	17	4	23.5	332	98.0	17	319	7	0	0
Piperacillin-tazobactam Enterobacterales[^] [Breakpoints (µg/mL): ≤8/4 (S), 16/4 (I), ≥32/4 (R)]													
Seeded Challenge	47	43	91.5	12	8	66.7	42	89.4	18	28	3	2	0
Seeded Clinical	195	189	97.0	14	8	57.4	187	96.0	2	192	7	1	0
Combined	242	232	95.9	26	16	61.5	229	94.6	20	220	10	3	0
Trimethoprim-sulfamethoxazole Enterobacterales[^] [Breakpoints (µg/mL): ≤2 (S), ≥4 (R)]													
Seeded Challenge	43	41	95.3	4	2	50	42	97.7	38	5	0	0	0**
Seeded Clinical	122	122	100	2	2	100	122	100	11	111	0	0	0
Combined	165	163	98.8	6	4	66.7	164	99.4	49	116	0	0	0**

*SDD- Susceptible-dose dependent.

** Adjusted VMJ

[^] Some species within Enterobacterales had mostly off-scale results due to current epidemiology and/or device design.

One very major error (VMJ) was observed with ceftazidime when testing *Morganella morganii* that resulted in an unacceptable VMJ rate (16.7%, 1/6). This was considered random due to the limited number of resistant *Morganella morganii* isolates tested.

EA - Essential Agreement

R - Resistant isolates

min - minor errors

CA - Category Agreement

S - Susceptible isolates

maj - major errors

Eval - Evaluable isolates

vmj - very major errors

Trending

A trending analysis on sample results was conducted to evaluate antimicrobial/organism combinations for which LifeScale Gram Negative Kit (LSGN) MIC results were determined to be one or more doubling dilutions lower or higher than the reference result (Table 5). MIC results that were off-scale for both the reference and LifeScale Gram Negative Kit (LSGN) were not considered in the trending analysis. Antimicrobial/organism combinations for which the difference between the percentage of isolates with higher or lower MIC values was $\geq 30\%$ with a statistically significant confidence interval were considered to have evidence of trending and is addressed in the labeling.

Table 5. LifeScale Gram Negative Kit (LSGN) – Analysis of Trending in the Clinical Study

Drug	Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted in the Clinical Study
Ampicillin	<i>P. mirabilis</i>	13	2, (15.4)	0	11 (84.6)	69%, (31%, 85%)	Yes
	<i>Salmonella spp.</i>	9	0, (0)	1	8, (88.9)	89%, (45%, 98%)	Yes
Aztreonam	<i>C. freundii</i>	22	1, (4.6)	3	18, (81.8)	77%, (51%, 89%)	Yes
	<i>C. koseri</i>	8	1, (12.5)	1	6, (75)	62%, (14%, 83%)	Yes
	<i>E. cloacae</i> complex	16	3, (18.8)	5	8, (50)	31%, (-1%, 56%)	No
	<i>M. morganii</i>	19	4, (21.1)	3	12, (63.2)	42%, (11%, 64%)	Yes
	<i>P. mirabilis</i>	26	0, (0)	0	26, (100)	100% (82%, 100%)	Yes
	<i>P. vulgaris</i>	17	0, (0)	1	16, (94.1)	94% (66%, 99%)	Yes
	<i>Pr. rettgeri</i>	5	0, (0)	1	4, (80)	80% (19%, 96%)	Yes
	<i>Pr. stuartii</i>	1	0, (0)	0	1, (100)	100%, (-12%, 100%)	No
	<i>S. marcescens</i>	12	1, (8.3)	2	9, (75)	67%, (28%, 84%)	Yes
Cefepime	<i>C. freundii</i>	18	5, (27.8)	1	12, (66.7)	39%,	Yes

Drug	Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted in the Clinical Study
						(6%, 62%)	
	<i>E. cloacae</i> complex	14	5, (35.7)	0	9, (64.3)	29%, (-8%, 56%)	No
	<i>M. morganii</i>	22	4, (18.2)	2	16, (72.7)	55%, (25%, 72%)	Yes
	<i>P. mirabilis</i>	22	2, (9.1)	0	20, (90.9)	82%, (55%, 91%)	Yes
	<i>P. vulgaris</i>	14	0, (0)	1	13, (92.9)	93%, (60%, 99%)	Yes
	<i>Pr. rettgeri</i>	2	1, (50)	0	1, (50)	0%, (-57%, 57%)	No
	<i>Pr. stuartii</i>	7	1, (14.3)	1	5, (71.4)	57%, (6%, 81%)	Yes
	<i>S. marcescens</i>	42	1, (2.4)	0	41, (97.6)	95%, (81%, 98%)	Yes
Ceftazidime	<i>C. freundii</i>	9	6, (66.67)	0	3, (33.33)	-33%, (-63%, 11%)	No
	<i>C. koseri</i>	24	1, (4.17)	0	23, (95.83)	92%, (69%, 97%)	Yes
	<i>E. cloacae</i> complex	10	6, (60)	1	3, (30)	-30%, (-60%, 12%)	No
	<i>M. morganii</i>	15	7, (46.67)	6	2, (13.33)	-33%, (-58%, 0%)	Yes
	<i>P. mirabilis</i>	25	1, (4)	0	24, (96)	92%, (70%, 97%)	Yes
	<i>P. vulgaris</i>	18	0, (0)	1	17, (94.44)	94%, (68%, 99%)	Yes
	<i>Pr. stuartii</i>	9	1, (11.11)	0	8, (88.89)	78%, (32%, 91%)	Yes
	<i>S. marcescens</i>	47	1, (2.13)	2	44, (93.62)	91%, (77%, 96%)	Yes
Ceftazidime- avibactam	<i>C. freundii</i>	6	0, (0)	0	6, (100)	100%, (45%, 100%)	Yes
	<i>C. koseri</i>	13	3, (23.08)	1	9, (69.23)	46%, (8%, 70%)	Yes
	<i>E. cloacae</i> complex	6	1, (16.67)	0	5, (83.33)	67%, (11%, 86%)	Yes
	<i>M. morganii</i>	6	0, (0)	0	6, (100)	100%, (45%, 100%)	Yes

Drug	Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted in the Clinical Study
	<i>P. mirabilis</i>	4	0, (0)	0	4, (100)	100%, (31%, 100%)	Yes
	<i>Pr. rettgeri</i>	1	0, (0)	0	1, (100)	100%, (-12%, 100%)	No
	<i>Pr. stuartii</i>	0	0,0	0	0,0	0	NA
	<i>S. marcescens</i>	47	0, (0)	1	46, (97.87)	98%, (86%, 100%)	Yes
Ertapenem	<i>C. freundii</i>	25	4, (16)	1	20, (80)	64%, (37%, 79%)	Yes
	<i>C. koseri</i>	12	4, (33.33)	0	8, (66.67)	33%, (-6%, 61%)	No
	<i>E. cloacae</i> complex	15	3, (20)	1	11, (73.33)	53%, (18%, 74%)	Yes
	<i>M. morganii</i>	15	0, (0)	1	14, (93.33)	93%, (62%, 99%)	Yes
	<i>Pr. rettgeri</i>	3	1, (33.33)	0	2, (66.67)	33%, (-32%, 72%)	No
	<i>Pr. stuartii</i>	0	0,0	0	0,0	0	NA
	<i>S. marcescens</i>	24	6, (25)	0	18, (75)	50%, (22%, 68%)	Yes
Gentamicin	<i>C. freundii</i>	7	2, (28.57)	0	5, (71.43)	43%, (-7%, 72%)	No
	<i>C. koseri</i>	5	2, (40)	0	3, (60)	20%, (-32%, 60%)	No
	<i>E. cloacae</i> complex	4	0, (0)	2	2, (50)	50%, (-10%, 85%)	No
	<i>S. marcescens</i>	28	5, (17.86)	2	21, (75)	57%, (32%, 73%)	Yes
Levofloxacin	<i>C. freundii</i>	17	2, (11.76)	6	9, (52.94)	41%, (10%, 64%)	Yes
	<i>C. koseri</i>	8	1, (12.5)	5	2, (25)	12%, (-26%, 48%)	No
	<i>E. cloacae</i> complex	10	2, (20)	0	8, (80)	60%, (16%, 80%)	Yes
	<i>M. morganii</i>	7	0, (0)	2	5, (71.43)	71%, (21%, 92%)	Yes
	<i>P. mirabilis</i>	16	0, (0)	2	14, (87.5)	88%, (57%, 97%)	Yes
	<i>P. vulgaris</i>	10	1, (10)	1	8, (80)	70%, (27%, 87%)	Yes

Drug	Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted in the Clinical Study
	<i>Pr. rettgeri</i>	9	0, (0)	2	7, (77.78)	78%, (34%, 94%)	Yes
	<i>Pr. stuartii</i>	7	1, (14.29)	2	4, (57.14)	43%, (-6%, 72%)	No
	<i>S. marcescens</i>	51	2, (3.92)	7	42, (82.35)	78%, (63%, 87%)	Yes
Meropenem	<i>C. freundii</i>	8	4, (50)	0	4, (50)	0%, (-40%, 40%)	No
	<i>C. koseri</i>	17	5, (29.41)	0	12, (70.59)	41%, (8%, 64%)	Yes
	<i>E. cloacae</i> complex	17	7, (41.18)	1	9, (52.94)	12%, (-20%, 40%)	No
	<i>P. mirabilis</i>	13	3, (23.08)	0	10, (76.92)	54%, (15%, 75%)	Yes
	<i>S. marcescens</i>	16	4, (25)	0	12, (75)	50%, (15%, 71%)	Yes
Meropenem/ vaborbactam	<i>C. freundii</i>	16	3, (18.75)	1	12, (75)	56%, (22%, 75%)	Yes
	<i>C. koseri</i>	11	2, (18.18)	0	9, (81.82)	64%, (22%, 82%)	Yes
	<i>E. cloacae</i> complex	17	3, (17.65)	0	14, (82.35)	65%, (32%, 81%)	Yes
	<i>M. morganii</i>	19	0, (0)	0	19, (100)	100%, (76%, 100%)	Yes
	<i>P. mirabilis</i>	6	2, (33.33)	0	4, (66.67)	33%, (-19%, 67%)	No
	<i>Pr. rettgeri</i>	4	1, (25)	0	3, (75)	50%, (-14%, 79%)	No
	<i>Pr. stuartii</i>	1	0, (0)	0	1, (100)	100%, (-12%, 100%)	No
	<i>S. marcescens</i>	8	4, (50)	0	4, (50)	0%, (-40%, 40%)	No
Piperacillin/ tazobactam	<i>C. koseri</i>	33	2, (6.06)	3	28, (84.85)	79%, (58%, 88%)	Yes
	<i>P. mirabilis</i>	21	0, (0)	2	19, (90.48)	90%, (66%, 97%)	Yes
	<i>P. vulgaris</i>	20	0, (0)	0	20, (100)	100%, (77%, 100%)	Yes
	<i>Pr. rettgeri</i>	5	0, (0)	0	5, (100)	100%, (39%,	Yes

Drug	Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted in the Clinical Study
						100%	
	<i>Pr. stuartii</i>	3	2, (66.67)	0	1, (33.33)	-33%, (-72%, 32%)	No
	<i>S. marcescens</i>	28	2, (7.14)	3	23, (82.14)	75%, (51%, 86%)	Yes
Trimethoprim- sulfamethoxazole	<i>E. cloacae</i> complex	7	5, (71.43)	1	1, (14.29)	-57%, (-81%, -6%)	Yes
	<i>M. morgani</i>	8	2, (25)	1	5, (62.5)	38%, (-9%, 67%)	No
	<i>P. mirabilis</i>	24	5, (20.83)	1	18, (75)	54%, (26%, 72%)	Yes
	<i>P. vulgaris</i>	15	7, (46.67)	0	8, (53.33)	7%, (-26%, 38%)	No

Analysis of trending in the clinical study indicated that LifeScale Gram Negative Kit (LSGN) MIC values for the following antimicrobial/organism combinations tended to be at least one doubling dilution higher than the reference MIC value:

- Ampicillin: *P. mirabilis*, *Salmonella* spp.
- Aztreonam: *C. freundii*, *C. koseri*, *M. morgani*, *P. mirabilis*, *P. vulgaris*, *Pr. rettgeri*, *S. marcescens*
- Cefepime: *C. freundii*, *M. morgani*, *P. mirabilis*, *P. vulgaris*, *Pr. stuartii*, *S. marcescens*
- Ceftazidime: *C. koseri*, *P. mirabilis*, *P. vulgaris*, *Pr. stuartii*, *S. marcescens*
- Ceftazidime-avibactam: *C. freundii*, *C. koseri*, *E. cloacae* complex, *M. morgani*, *P. mirabilis*, *S. marcescens*
- Ertapenem: *C. freundii*, *E. cloacae* complex, *M. morgani*, *S. marcescens*
- Gentamicin: *S. marcescens*
- Levofloxacin: *C. freundii*, *E. cloacae* complex, *M. morgani*, *P. mirabilis*, *P. vulgaris*, *Pr. rettgeri*, *S. marcescens*
- Meropenem: *C. koseri*, *P. mirabilis*, *S. marcescens*
- Meropenem-vaborbactam: *C. freundii*, *C. koseri*, *E. cloacae* complex, *M. morgani*
- Piperacillin-tazobactam: *C. koseri*, *P. mirabilis*, *P. vulgaris*, *Pr. rettgeri*, *S. marcescens*
- Trimethoprim-sulfamethoxazole: *P. mirabilis*

LifeScale Gram Negative Kit (LSGN) MIC values for the following antimicrobial/organism combinations tended to be at least one doubling dilution lower than the reference MIC value:

- Ceftazidime: *M. morgani*

- *Trimethoprim-sulfamethoxazole: E. cloacae complex*

To address the overall observed trending with the LifeScale Gram Negative Kit (LSGN) in the clinical study, the following statement was added to the device labeling:

In the clinical study, the majority of drug/organism combinations tested with the LifeScale Gram Negative Kit (LSGN) showed MIC values equal to or at least one doubling dilution higher than the reference method. Use caution when reporting drug resistance for any antimicrobial. The following drug/organism combinations showed high trending:

The following drug/organism combinations showed high trending:

- *Ampicillin: P. mirabilis, Salmonella spp.*
- *Aztreonam: C. freundii, C. koseri, E. cloacae complex, M. morganii, P. mirabilis, P. vulgaris, Pr. rettgeri, Pr. stuartii, S. marcescens*
- *Cefepime: C. freundii, M. morganii, P. mirabilis, P. vulgaris, Pr. stuartii, S. marcescens*
- *Ceftazidime: C. koseri, P. mirabilis, P. vulgaris, Pr. stuartii, S. marcescens*
- *Ceftazidime-avibactam: C. freundii, C. koseri, E. cloacae complex, M. morganii, P. mirabilis, Pr. rettgeri, S. marcescens*
- *Ertapenem: C. freundii, C. koseri, E. cloacae complex, M. morganii, Pr. rettgeri, S. marcescens*
- *Gentamicin: C. freundii, E. cloacae complex, S. marcescens*
- *Levofloxacin: C. freundii, E. cloacae complex, M. morganii, P. mirabilis, P. vulgaris, Pr. rettgeri, Pr. stuartii, S. marcescens*
- *Meropenem: C. koseri, P. mirabilis, S. marcescens*
- *Meropenem-vaborbactam: C. freundii, C. koseri, E. cloacae complex, M. morganii, P. mirabilis, Pr. rettgeri, Pr. stuartii*
- *Piperacillin-tazobactam: C. koseri, P. mirabilis, P. vulgaris, Pr. rettgeri, S. marcescens*
- *Trimethoprim-sulfamethoxazole: M. morganii, P. mirabilis*

The following drug/organism combinations showed low trending:

- *Ceftazidime: C. freundii, E. cloacae complex, M. morganii,*
- *Piperacillin-tazobactam: Pr. stuartii*
- *Trimethoprim-sulfamethoxazole: E. cloacae complex*

Additional Testing to Address Limitations included in K211815 and K241324

Additional clinical testing was performed to address limitations in the LifeScale Gram Negative Kit (LSGN) with the LifeScale AST System device labeling for previously cleared antimicrobial/organism combinations in K211815 and K241324.

Aztreonam/P. aeruginosa.

In K211815, evaluation of performance for aztreonam/*P. aeruginosa* demonstrated unacceptable performance due to a high very major error rate (3.7%, 2/54 resistant isolates). To address this unacceptable very major error rate, the following limitation was included in the device labeling:

Perform an alternative method of testing prior to reporting results for the following antimicrobial/organism combination: Aztreonam/P. aeruginosa

In the current submission, an additional 69 *P. aeruginosa* samples were evaluated with aztreonam and combined with the original data submitted in K211815 for a total of 185 results. Combined results are shown in Table 6 below. Combined testing demonstrated an EA of 96.2% and CA of 90.8%. There were 14 (7.8%) minor, one major (1.4%, 1/73) and two very major errors (2.0%, 2/101). This performance is acceptable and the limitation for aztreonam/*P. aeruginosa* was removed from the device labeling.

Table 6. Performance for Aztreonam/*P. aeruginosa*

Aztreonam <i>P. aeruginosa</i> [Breakpoints (µg/mL): ≤8 (S), 16 (I), ≥32 (R)]													
	Tot	No. EA	EA %	Eva I EA Tot	No. Eva I EA	Eva I EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
Prospective	15	14	93.3	14	13	92.9	14	93.3	2	12	0	1	0
Seeded Challenge	113	113	100	60	60	100	106	93.8	78	29	7	0	0
Seeded Clinical	57	51	89.5	55	49	89.1	48	84.2	21	32	7	0	2
Combined	185	178	96.2	129	122	94.6	168	90.1	101	73	14	1	2

Ceftazidime-avibactam/*K. pneumoniae*.

In K241324, evaluation of performance for ceftazidime-avibactam/*K. pneumoniae* showed unacceptable performance due to a high adjusted very major error rate (5.0%, 1/20). To address this unacceptable adjusted very major error rate, the following limitation was included in the device labeling:

Perform an alternative method of testing prior to reporting results for the following antimicrobial/organism combination: Ceftazidime-avibactam/K. pneumoniae

In the current submission, an additional 31 *K. pneumoniae* samples were evaluated with ceftazidime-avibactam and combined with the original data submitted in K241324 for a total of 173 results. Combined testing results demonstrated an EA of 98.8% and CA of 98.3%. There was one major (1.6%, 2/123) and one very major error (2.0%, 1/50). Due to the lack of an intermediate breakpoint, further analysis of the errors was performed, and adjustments were made by considering the MIC values of the errors compared to the reference MIC values. One of the major errors was in essential agreement with the reference MIC values. Therefore, the major error rate was adjusted to 0.8% (1/123). The very major error was not in essential agreement with the reference MIC. Therefore, the adjusted very major error rate remains 2.0% (1/50). This performance is acceptable and the limitation for ceftazidime-avibactam/*K. pneumoniae* was removed from the device labeling. The *LifeScale LSGN Clinical Performance* table has been updated in the device labeling.

Re-analysis of Clinical Data with Updated Breakpoints

Since the clearance of K211815 and K241324, FDA-recognized breakpoints for cefepime, ceftazidime, and piperacillin-tazobactam with *P. aeruginosa* have been updated. The original clinical data was re-analyzed, and performance was assessed with the updated breakpoints.

Cefepime/*Pseudomonas aeruginosa*

Clinical data collected for cefepime/*Pseudomonas aeruginosa* in K241324 was re-analyzed with updated breakpoints (Table 7).

Table 7. Updated Breakpoints for Cefepime/*Pseudomonas aeruginosa*

Cefepime/<i>P. aeruginosa</i>				
Breakpoints (µg/mL)	S	SDD	I	R
Previous	≤8	-	-	≥16
Current	≤8	-	16	≥32

Using the original breakpoints, data demonstrated an EA of 93.1% and a CA of 84.2%. The CA was considered acceptable as the EA of evaluable results is 91.0%. There were 13 major errors (18.1%) and 3 very major errors (10.3%). Due to a lack of an intermediate breakpoint, further analysis of the errors was performed, and adjustments were made by considering the MIC values of the errors compared to the reference MIC value. Eleven of the major errors were in essential agreement with the reference MIC value. Therefore, the major error rate and very major error rate were adjusted to 2.8% (2/72) and 10.3% (3/29), respectively, which was still unacceptable. To address this unacceptable very major error rate, the following limitation was included in the device labeling:

Perform an alternative method of testing prior to reporting results for:

- *Cefepime: P. aeruginosa when the LifeScale MIC is 4 µg/mL due to the occurrence of very major errors (3/29 resistant isolates, 10.34%)*

Using the updated breakpoints, data demonstrated an EA of 93.1%, which is acceptable, and a CA of 80.2%. The CA is considered acceptable as the EA of evaluable results is 91.0%. There were 19 minor errors, no major errors, and one very major (4.8%, 1/21) error. This very major error rate is unacceptable. The limitation is updated in the device labeling to the following to reflect the updated performance:

Perform an alternative method of testing prior to reporting results for:

- *Cefepime: P. aeruginosa when the LifeScale MIC is 4 µg/mL due to the occurrence of very major errors (1/21 resistant isolates, 4.8%)*

Ceftazidime/*Pseudomonas aeruginosa*

Clinical data collected for ceftazidime/*Pseudomonas aeruginosa* in K211815 was re-analyzed with updated breakpoints (Table 8).

Table 8. Updated Breakpoints for Ceftazidime/*Pseudomonas aeruginosa*

Ceftazidime/<i>P. aeruginosa</i>				
Breakpoints (µg/mL)	S	SDD	I	R
Previous	≤8	-	-	≥16
Current	≤8	-	16	≥32

Using the original breakpoints, data demonstrated an EA of 92.2% and a CA of 94.0%, which was acceptable. There were five major errors (8.2%) and 2 very major errors (3.6%). Due to a lack of an intermediate breakpoint, further analysis of the errors was performed, and adjustments were made by considering the MIC values of the errors compared to the reference MIC value. One of the very major errors were in essential agreement with the reference MIC value. Therefore, the very major error rate was adjusted to 1.8%, which was acceptable. Two of the major errors were in essential agreement with the reference MIC value. Therefore, the major error rate was adjusted to 3.3%, which was still unacceptable. To address the unacceptable adjusted major error rate, the following limitation was included in the device labeling:

Perform an alternative method of testing prior to reporting results for:

- *Ceftazidime: *P. aeruginosa* at MIC value of 16 µg/mL due to the occurrence of major errors (5/61 susceptible isolates, 8.2%) adjusted to 2 major errors (3.3%) due to lack of an intermediate breakpoint.*

Using the updated breakpoints, data demonstrated an EA of 92.2% and a CA of 90.0%, which is acceptable. There were 11 minor, no major, and one (1.9%, 1/52) very major errors. This performance is acceptable (Table 9) and the limitation for ceftazidime/*Pseudomonas aeruginosa* was removed from the device labeling.

Table 9. Performance for Ceftazidime/*P. aeruginosa*

Ceftazidime <i>P. aeruginosa</i> [Breakpoints (µg/mL): ≤8 (S), 16 (I), ≥32 (R)]													
	Tot	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
Prospective	15	15	100	12	12	100	14	93.3	1	13	1	0	0
Seeded Challenge	55	54	98.2	30	29	96.7	55	100	36	18	0	0	0
Seeded Clinical	46	38	82.6	43	35	81.4	35	76.1	15	30	10	0	1
Combined	116	107	92.2	85	76	89.4	104	90.0	52	61	11	0	1

Piperacillin-tazobactam/*P. aeruginosa*

Clinical data collected for piperacillin/*Pseudomonas aeruginosa* in K241324 was re-analyzed with updated breakpoints (Table 10).

Table 10. Updated Breakpoints for Piperacillin-tazobactam/*Pseudomonas aeruginosa*

Piperacillin-tazobactam/<i>P. aeruginosa</i>				
Breakpoints (µg/mL)	S	SDD	I	R
Previous	≤8/4	16/4	-	≥32/4
Current	≤16/4	-	32/4	≥64/4

Using the original breakpoints, data demonstrated an EA of 94.1% and a CA of 93.5%, which was acceptable. There was one major error (0.9%) and one very major error (1.5%).

Using the updated breakpoints, data demonstrated an EA of 94.1% and a CA of 93.0%, which is considered acceptable. There were 11 minor, one (0.9%, 1/118) major, and one (1.7%, 1/60) very major error. This performance is acceptable (Table 11) and the *LifeScale LSGN Clinical Performance* table has been updated in the device labeling.

Table 11. Performance for Piperacillin-tazobactam/*P. aeruginosa*

Piperacillin-tazobactam <i>P. aeruginosa</i> [Breakpoints (µg/mL): ≤16/4 (S), 32/4 (I), ≥64/4 (R)]													
	Tot	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	min	maj	vmj
Prospective	15	15	100	5	5	100	12	80	2	13	3	0	0
Seeded Challenge	114	110	96.5	28	24	85.7	111	97.4	42	69	3	0	0
Seeded Clinical	56	49	87.5	26	19	73.1	49	87.5	16	36	5	1	1
Combined	185	174	94.1	59	48	81.4	172	93.0	60	118	11	1	1

Amikacin/*P. aeruginosa*

The current FDA STIC-recognized breakpoints can only be reported for amikacin/*P. aeruginosa* on organisms isolated from the urinary tract. Since this device reports results for organisms isolated from positive blood cultures, it is inappropriate to report results for amikacin/*P. aeruginosa*. Therefore, the device labeling has been updated to remove any claims or limitations related to amikacin/*P. aeruginosa*.

Gentamicin/*P. aeruginosa*

There are no longer FDA STIC-recognized breakpoints for gentamicin/*P. aeruginosa*. Therefore, the device labeling has been updated to remove any claims or limitations related to gentamicin/*P. aeruginosa*.

Testing/Reporting MICs for Species Not Listed in the Indications for Use

For this review, the interpretive criteria are applied to the organisms/organism groups according to the FDA STIC website. As required under 511A(2)(2)(B) of the Federal Food, Drug and Cosmetic Act, the following statement is included in the General Precautions section of the device labeling to address testing and reporting of species not listed in the Indications for Use:

The safety and efficacy of antimicrobial drugs, for which antimicrobial susceptibility is tested by this AST device, may or may not have been established in adequate and well controlled clinical trials for treating clinical infections due to microorganisms outside of those found in the indications and usage in the drug label. The clinical significance of susceptibility information in those instances is unknown. The approved labeling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.

2. Matrix Comparison:

Not applicable

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Antimicrobial	Organism	Interpretive Criteria ^a			
		S	SDD	I	R
Amikacin	<i>Acinetobacter</i> spp.	≤16	-	32	≥64
Ampicillin	Enterobacterales	≤8	-	16	≥32
	<i>Salmonella</i> spp				
Aztreonam	Enterobacterales	≤4	-	8	≥16
	<i>P. aeruginosa</i>	≤8	-	16	≥32
Cefazolin	Enterobacterales	≤2	-	4	≥8
Ceftazidime	<i>Acinetobacter</i> spp.	≤8	-	16	≥32
	Enterobacterales	≤4	-	8	≥16
	<i>P. aeruginosa</i>	≤8	-	16	≥32
Cefepime	Enterobacterales	≤2	4-8	-	≥16
	<i>P. aeruginosa</i>	≤8	-	16	≥32
Ceftazidime-avibactam	Enterobacterales	≤8/4	-	-	≥16/4
Ertapenem	Enterobacterales	≤0.5	-	1	≥2

Gentamicin	Enterobacterales	≤ 2	-	4	≥ 8
Levofloxacin	Enterobacterales	≤ 0.5	-	1	≥ 2
	<i>P. aeruginosa</i>	≤ 1	-	2	≥ 4
Meropenem	Enterobacterales	≤ 1	-	2	≥ 4
	<i>P. aeruginosa</i>	≤ 2	-	4	≥ 8
	<i>Acinetobacter</i> spp.				
Meropenem-vaborbactam	Enterobacterales	$\leq 4/8$	-	8/8	$\geq 16/8$
Piperacillin-tazobactam	Enterobacterales	$\leq 8/4$	-	16/4	$\geq 32/4$
	<i>P. aeruginosa</i>	$\leq 16/4$	-	32/4	$\geq 64/4$
	<i>Acinetobacter</i> spp.	$\leq 16/4$	-	32/4-64/4	$\geq 128/4$
Trimethoprim-Sulfamethoxazole	Enterobacterales	$\leq 2/38$	-	-	$\geq 4/76$

S = Susceptible; SDD = Susceptible-dose dependent; I = Intermediate; R = Resistant

^a FDA-Recognized Antimicrobial Susceptibility [Website](#)

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission included a predetermined change control plan (PCCP) with a breakpoint change protocol that was reviewed and accepted by FDA in submission K211815 cleared on April 02, 2024. This protocol addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm>). The protocol outlined the specific procedures and acceptance criteria that Affinity Biosensors intends to use to evaluate the LifeScale AST system with the LifeScale Gram Negative Kit (LSGN) when revised breakpoints for indicated drugs are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, Affinity Biosensors will update the LifeScale AST system LifeScale Gram Negative Kit (LSGN) label to include (1) the new breakpoints, (2) an updated performance section after re-evaluation of data in this premarket notification with the new breakpoints, and (3) any new limitations as determined by their evaluation.