October 27, 2025

Affinity Biosensors, LLC
Nicole Holliday
Director of Clinical Studies
222 East Canon Perdido Street
Santa Barbara, California 93101

Re: K251875
Trade/Device Name: LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system
Regulation Number: 21 CFR 866.1650
Regulation Name: A Cellular Analysis System For Multiplexed Antimicrobial Susceptibility
Regulatory Class: Class II
Product Code: SAN, LON
Dated: September 25, 2025
Received: September 25, 2025

Dear Nicole Holliday:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not

required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ribhi Shawar -S

Ribhi Shawar, Ph.D. (ABMM)
Branch Chief, General Bacteriology and Antimicrobial Susceptibility Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K251875

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

Indications for Use *(Describe)*
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.

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)

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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K251875
510(k) Substantial Equivalence Determination Performance Summary
In Compliance with Section 807.92(c)

1. Contact Details

Submitter:
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2. Device

Name of Device: LifeScale™ Gram Negative Kit (LSGN) with the LifeScale AST system
Common or Usual Name: LifeScale AST system

Regulation Name:
A cellular analysis system for multiplexed antimicrobial susceptibility testing

Regulation Number:
21 CFR 866.1650

Regulatory Class:
Class II

Product Code:
SAN, LON

Predicate Device:
K211815/K241324 LifeScale™ Gram Negative Kit (LSGN) with the LifeScale AST system

Purpose for Submission:

i. To obtain a substantial equivalence determination for the addition of the following gram-negative non-fastidious organisms to the LifeScale Gram Negative Kit (LSGN) Kit: Amikacin, Ampicillin, Aztreonam, Cefazolin, Cefepime, Ceftazidime, Ceftazidime-avibactam, Ertapenem, Gentamicin, Levofloxacin, Meropenem, Meropenem-vaborbactam, Piperacillin-tazobactam, Trimethoprim-sulfamethoxazole. The LSGN Kit is used with the LifeScale AST system for testing positive blood culture samples containing gram-negative bacilli.

Antimicrobial/Organism Combinations with Less Prevalent 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. (other than Acinetobacter ursingii),* 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.,* 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.,* 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)*

Cleared Antimicrobial/Organism Combinations (K211815):

1. **Ampicillin:** *Escherichia coli*
2. **Aztreonam:** *Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca*
3. **Cefazolin:** *Klebsiella pneumoniae, Klebsiella variicola*
4. **Ceftazidime:** *Acinetobacter baumannii, Acinetobacter baumannii/nosocomialis group, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella variicola, Pseudomonas aeruginosa*
5. **Ertapenem:** *Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca*
6. **Trimethoprim-Sulfamethoxazole**: *Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella variicola*

Additional Claimed Antimicrobial/Organism Combinations (K241324):

7. **Amikacin:** *Acinetobacter* spp.*, Escherichia coli, Klebsiella pneumoniae, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella variicola, Pseudomonas aeruginosa*
8. **Cefepime:** *Escherichia coli, Klebsiella pneumoniae, Klebsiella aerogenes, Klebsiella oxytoca, Pseudomonas aeruginosa*
9. **Ceftazidime-avibactam:** *Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca*
10. **Gentamicin:** *Escherichia coli, Klebsiella pneumoniae, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella variicola, Pseudomonas aeruginosa*
11. **Levofloxacin:** *Escherichia coli, Klebsiella pneumoniae, Klebsiella aerogenes, Klebsiella oxytoca, Pseudomonas aeruginosa*
12. **Meropenem:** *Acinetobacter* spp.*, Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Pseudomonas aeruginosa*
13. **Meropenem-vaborbactam:** *Escherichia coli, Klebsiella pneumoniae, Klebsiella aerogenes, Klebsiella oxytoca*
14. **Piperacillin-tazobactam:** *Acinetobacter* spp.*, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*

ii. Limitation Removal/Update Breakpoints

Removal of limitations included in the cleared LifeScale LSGN Kit with the LifeScale AST system (K241324). See limitation Removal Report for data analysis.

	Antimicrobial/Organism	Current Limitation	Corrective Action In K251875 Labeling
2.	Ceftazidime-avibactam/*K. pneumoniae*	*Perform an alternative method of testing prior to reporting results for the following antimicrobial/organism combination(s): Ceftazidime-avibactam/K. pneumoniae*	*Additional clinical testing and revised limitation*
3.	Aztreonam/*P. aeruginosa*	*Perform an alternative method of testing prior to reporting results for the following antimicrobial/organism combination(s): Aztreonam/P.aeruginosa*	*Additional clinical testing and revised limitation*
4.	Cefepime/*P. aeruginosa*	***Update Breakpoints*** ***Current Limitation:*** *Perform an alternate method of testing prior to reporting P.aeruginosa when the MIC is 4 µg/mL due to the occurrence of very major errors (3/29 resistant isolates, 10.34%).*	***Limitation Revision:*** *Perform an alternate method of testing prior to reporting P.aeruginosa when the MIC is 4 µg/mL due to the occurrence of a very major error (1/21 resistant isolates error (4.7%).* *Updated FDA/CLSI Breakpoints and revised in labeling*
5.	Ceftazidime/*P. aeruginosa*	***Update breakpoints*** ***Current Limitation:*** *Perform an alternative method of testing prior to reporting 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 a lack of an intermediate*	***Remove Limitation*** *Updated FDA/CLSI Breakpoints and revised in labeling*

6.	Piperacillin-tazobactam/*P. aeruginosa*	***Update Breakpoints***	*Updated FDA/CLSI Breakpoints and revised in labeling*

Antimicrobials:

Table 1. LifeScale LSGN Antimicrobials and Reportable Ranges

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**

Test Type:

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.

3. Device Description

The Affinity Biosensors LifeScale Gram Negative Kit (LSGN) 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-defined or 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 LSGN Kit. Preliminary results are available in most cases within four hours from initiation of the assay.

4. Intended Use/Indications for Use

Intended Use:

The LifeScale AST system is a multiplexed *in vit*ro 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/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 and for epidemiologic testing and for recovery of organisms present in microbial samples.

New Indications 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)***

5. Substantial Equivalence

This submission is an addition of claims to the K211815/K241324 and does not impact the safety or effectiveness of the LifeScale AST system.

Device & Predicate Device(s):	**New Device** **Affinity Biosensors Lifescale Gram Negative Kit (LSGN) with the LifeScale AST system**	**K241324** **Predicate Device** **Affinity Biosensors Lifescale Gram Negative Kit (LSGN) with the LifeScale AST system**
Device Trade Name	Lifescale Gram Negative Kit (LSGN) with the LifeScale AST system	Lifescale Gram Negative Kit (LSGN) with the LifeScale AST system
General Device Similarities		
Intended Use/Indications for Use	The LifeScale AST system is a multiplexed *in vit*ro 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, for epidemiologic testing and for recovery of organisms present in microbial samples. The LifeScale Gram Negative Kit (LSGN) is intended for use with the LifeScale AST system for *in vitro* testing of positive blood culture samples confirmed by Gram stain as containing gram-negative bacilli.	Same
Sample	Blood cultures are signaled as positive by a continuous monitoring blood culture system.	Same
Inoculation Method	Automated	Same
Read Method	Automated	Same
Results	Report results as a minimum inhibitory concentration (MIC) and categorical interpretation (S, I/SDD, R)	Same

Sample Prep	Centrifugation and pipetting of sample.	Same
Inoculation Method	Automated	Same
IVD Functions	AST	Same
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
Differences		
Organisms Tested	*Acinetobacter spp.,* 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 rettgeri Providencia stuartii, Serratia marcescens), Pseudomonas aeruginosa, and Salmonella spp.*	*Acinetobacter spp.,* Enterobacterales *(Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Klebsiella variicola), and Pseudomonas aeruginosa*

6. Performance Characteristics

Comparison Study

A comparison study was conducted to evaluate the performance of the LifeScale Gram Negative Kit (LSGN) with the LifeScale AST system in testing clinical blood cultures confirmed positive by Gram Stain for Gram-negative bacilli. This study encompassed testing positive blood cultures (PBCs) contrived using contemporary and stock isolates chosen to generate data required to fulfill intended use claims. All LifeScale AST sample results were compared to the reference Broth Microdilution (BMD). Each sample submitted for BMD testing was assigned a unique Trial ID, and LifeScale results were kept blinded to prevent bias. Performance was evaluated by comparing quantitative (MIC) and qualitative (S/SDD/I/R) AST results generated by the LifeScale AST System with those of the reference BMD.

Positive Blood Cultures consistent with the inclusion criteria were enrolled and tested at 3 US Clinical sites. For testing samples, organism ID was performed using an FDA-cleared direct from positive blood culture ID system. Testing was performed on the LifeScale AST System in accordance with the indications for use. PBC bottles were sub-cultured onto Tryptic Soy Agar supplemented with 5% Sheep Blood panels (BAP) and MacConkey Agar panels (MAC) incubated for 18-24 hours and examined for purity and colony morphology. If more than one colony type was observed, each organism was isolated for purity. All organisms isolated were identified using matrix-assisted laser desorption/ionization (MALDI). Polymicrobial samples were withdrawn from the study. ID results generated using a direct from Blood Culture ID system and/or MALDI were entered into the LifeScale AST System, and a final MIC/SIR result was generated using the final LifeScale AST System software. If there was a discordant organism identification between MALDI and a Direct from Blood Culture system, MALDI ID was considered the organism's final identification.

Contrived samples were prepared from frozen isolates supplied by Affinity Biosensors, or they were prepared from contemporary/stock isolates collected by the laboratory and agreed upon by Affinity for study inclusion. Blood cultures with the required amount of blood were spiked with isolated organisms and incubated in the blood culture system. When flagged as positive, the positive blood culture was tested on the LifeScale AST system in accordance with manufacturer’s instructions for use. The PBC was sub-cultured to confirm purity. If a mixed (contaminated) culture was observed, a fresh contrived sample was prepared and tested.

All LifeScale system testing was performed within 12 hours of the blood culture bottle being flagged as positive. LifeScale panels were read upon system confirmation of growth. Positive growth was determined automatically by the LifeScale AST system as part of the reading process. If the panel was incubated offline, it would be placed on the LifeScale system to be read. To generate the final AST report, the organism ID was entered into LifeScale AST System. The LifeScale AST System software generated the final AST results (MIC and S/SDD/I/R).

Reference testing was performed on all enrolled samples in triplicate. Testing was done in accordance with the reference protocol and was performed at one trial site. Clinical sites shipped isolates on transport media from the PBC purity panel following verification of pure culture. Samples contrived from laboratory stock underwent organism identification using MALDI prior to shipping to the reference site for testing. Reference testing was performed in triplicate. The procedure for Broth Microdilution reference testing follows CLSI guidance (CLSI M07).

The performance of the LifeScale AST system with the LSGN Kit was compared to the FDA-recognized reference BMD method for determining quantitative (MIC) AST results direct from Gram-negative positive blood cultures. Acceptable clinical performance was assessed across the following parameters for each antimicrobial agent on the LSGN panel; Essential Agreement (EA), Category Agreement (CA), Essential Agreement of evaluable results (Evaluable EA), Very Major Discrepancy (VMJ), Major Discrepancy (MAJ), Minor Discrepancy (MIN), Growth Failure Rate. For drug/organism group combinations where the susceptible dose-dependent category is recognized in place of the intermediate category, any errors that were observed with this category were designated as minor errors. Assessment of categorical agreement (Susceptible/ Susceptible-Dose Dependent/Intermediate/Resistant) was conducted utilizing FDA breakpoints (Antimicrobial Susceptibility Test Interpretive Criteria/STIC) and CLSI M100 guidelines, if applicable.

Table 2. Number of Samples Tested

Sample Type	Total (% of Total)
Contemporary Isolates	240 (55.56%)
Stock Isolates	106 (24.54%)
Challenge Isolates	86 (19.91%)
Grand Total	**432 (100.0%)**

Exclusion Data

Summary of LifeScale LSGN AST Tests Initiated and Failed to Report a Result

The provided table summarizes tests initiated on the LifeScale AST system and the reasons for exclusion or incomplete results during clinical, analytical, and quality control (QC) phases. Out of 764 tests initiated:

Plate Failures (0.0%): This category includes issues such as being unable to verify positive controls, sensor clogs detected, and the system being unable to calculate MIC.
Growth Failures (0.26%): These failures occurred due to issues related to growth during testing.
LifeScale Failures (1.18%): This category involves failures directly attributable to the LifeScale system, including software and hardware failures.
Other Reasons (4.19%): This includes a variety of reasons such as operator errors, incubation time exceeding 8 hours, user cancellation, and protocol errors.

The total percentage of tests excluded, or incomplete, is 5.63%.

Reason for Exclusion/Incomplete Test	Clinical /Challenge	QC	Overall
Plate Failures*	[0/432] 0.0%	[0/332] 0.0%	[0/764] 0.0%
Growth Failures	[0/432] 0.0%	[2/332] 0.6%	[2/764] 0.26%
LifeScale Failures**	[6/432] 1.39%	[3/332] 0.9%	[9/764] 1.18%
Other Reasons***	[29/432] 6.71%	[3/332] 0.9%	[32/764] 4.19%
Total Excluded/Incomplete Tests	**[35/432] 8.1%**	**[8/332] 2.41%**	**[43/764] 5.63%**

Table 3. Summary of LifeScale LSGN AST tests initiated and failed to report a result

**Plate Failures include: unable to verify positive controls, sensor clog detected, system unable to calculate MIC*
***LifeScale Failures include: LifeScale system software and hardware failures*
****Other Reasons include: operator error, incubation time greater than 8 hours, user canceled, protocol error*

Clinical Performance Data

This interim report for performance represents the available clinical data for less prevalent organisms only. Data related to current Indications for Use organisms cleared in K211815/K241324; limitation removal and updated breakpoints will be incorporated once the FDA has completed it's evaluation of submitted reports. A finalized comprehensive version of this report, including all approved data sets and updates , will be issued following FDA feedback and included in the IFU.

Total Evaluated	No. EA	EA%	Eval Tot	No. Eval EA	Eval EA%	No. CA	CA%	No. R	No. S	#MIN (MIN%)	#MAJ (MAJ%)	#VMJ (VMJ%)
[a,e]**Ampicillin** - ***P. mirabilis*** **[Breakpoints (µg/mL): ≤8.0 (S),16, ≥32.0 (R)]**												
55	**54**	**98.2%**	**2**	**1**	**50.0%**	**55**	**100.0%**	**15**	**40**	**0 (0.00%)**	**0 (0.00%)**	**0 (0.00%)**
[a]**Ampicillin-*Salmonella spp.*** **[Breakpoints (µg/mL): ≤8.0 (S),16, ≥32.0 (R)]**												
20	**20**	**100%**	**1**	**1**	**100%**	**20**	**100%**	**3**	**17**	**0 (100%)**	**0 (100%)**	**0 (100%)**
[a,e]**Aztreonam – *C. freundii, C. koseri, E. cloacae complex M. morganii, P. mirabilis, P. vulgaris, P. rettgeri, P. stuartii, S. marcescens*** **[Breakpoints (µg/mL): ≤4.0 (S),8.0(I), ≥16.0 (R)]**												
365	**350**	**95.9%**	**42**	**27**	**64.3%**	**363**	**99.5%**	**47**	**316**	**2 (0.55%)**	**0 (0.00%)**	**0 (0.00%)**
[a,e]**Cefepime- *C. freundii, E. cloacae complex, M. morganii, P. mirabilis, P. vulgaris, P. rettgeri, P. stuartii, S. marcescens*** **[Breakpoints (µg/mL): ≤2 (S), 4,8 (SDD[b]), ≥16 (R)]**												
299	**289**	**96.7%**	**27**	**17**	**63.0%**	**293**	**98.0%**	**29**	**265**	**6 (2.01%)**	**0 (0.00%)**	**0 (0.00%)**
[a,e]**Ceftazidime - *C. freundii*, *C. koseri*, *E. cloacae complex, M.morganii, P.mirabilis, P.vulgaris, P.stuartii, S.marcescens*** **[Breakpoints (µg/mL): ≤4.0 (S), 8(I), ≥16.0 (R)]**												

346	327	94.5%	37	18	48.6%	336	97.1%	54	286	9 (2.60%)	0 (0.00%)	1 (1.85%)
[a,e]Ceftazidime-avibactam- *C. freundii*, *C. koseri*, *E. cloacae complex*, *M. morganii*, *P. mirabilis*, *P. rettgeri*, *P. stuartii*, *S. marcescens* [Breakpoints (µg/mL): ≤8/4 (S), ≥16/4 (R)]												
337	332	98.5%	9	4	44.4%	337	100.0%	20	317	0 (0.00%)	0 (0.00%)	0 (0.00%)
[a,e]Ertapenem - *C. freundii*, *C. koseri*, *E. cloacae complex*, *M. morganii*, *P. rettgeri*, *P. stuartii*, *S. marcescens* [Breakpoints (µg/mL): ≤0.5 (S),1(I), ≥2.0 (R)]												
278	263	94.6%	28	13	46.4%	268	96.4%	33	243	8 (2.88%)	2 (0.82%)	0 (0.00%)
[a,e]Gentamicin- *C. freundii*, *C. koseri*, *E. cloacae complex*, *S. marcescens* [Breakpoints (µg/mL): ≤2 (S), 4 (I), ≥8 (R)]												
206	205	99.5%	10	9	90.0%	202	98.1%	22	182	4(1.94%)	0(0.00%)	0(0.00%)
[a]Levofloxacin- *C. freundii*, *C. koseri*, *E. cloacae complex* *M. morganii*, *P. mirabilis*, *P. vulgaris*, *P. rettgeri*, *P. stuartii*, *S. marcescens* [Breakpoints (µg/mL): ≤0.5 (S), 1 (I), ≥2 (R)]												
371	359	96.8%	79	67	84.8%	348	93.8%	73	284	22 (5.93%)	1 (0.35%)	0 (0.00%)
[a,e]Meropenem- *C. freundii*, *C. koseri*, *E. cloacae complex*, *P. mirabilis*, *S. marcescens* [Breakpoints (µg/mL): ≤1 (S), 2 (I), ≥4 (R)]												
261	246	94.3%	23	8	34.8%	257	98.5%	25	234	4 (1.53%)	0 (0.00%)	0 (0.00%)
[a,e]Meropenem-vaborbactam- *C.freundii*, *C.koseri*, *E.cloacae complex*, *M.morganii*, *P.mirabilis*, *P.rettgeri*, *P.stuartii*, *S.marcescens* [Breakpoints (µg/mL): ≤4/8 (S), 8/8 (I), ≥16/8 (R)]												

339	**326**	**96.2%**	**17**	**4**	**23.5%**	**332**	**97.9%**	**17**	**319**	**7 (2.06%)**	**0 (0.00%)**	**0 (0.00%)**
[a,e]Piperacillin-tazobactam- *C.koseri, P.mirabilis, P.vulgaris, P.rettgeri, P.stuartii, S.marcescens* **[Breakpoints (µg/mL): ≤8/4 (S), 16/4 (I), ≥32/4 (R)]**												
242	**232**	**95.9%**	**26**	**16**	**61.5%**	**229**	**94.6%**	**20**	**220**	**10 (4.13%)**	**3 (1.36%)**	**0 (0.00%)**
[a,e]Trimethoprim-sulfamethoxazole - *E. cloacae complex, M. morganii P. mirabilis, P. vulgaris* **[Breakpoints (µg/mL): ≤2.0 (S), ≥4.0 (R)]**												
165	**163**	**98.8%**	**6**	**4**	**66.7%**	**164**	**99.4%**	**49**	**116**	**0 (0.00%)**	**0 (0.00%)**	**1 (2.04%)**

Table 4. ***LifeScale LSGN performance: Interpretation of MIC results are based on FDA Susceptibility Test Interpretative Criteria (STIC) and the 35th edition of the CLSI M100***

[a]In the clinical study, the majority of drug/organism combinations tested with the LifeScale LSGN with the LifeScale AST system 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:

Trending

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 *- E. coli, Proteus mirabilis and Salmonella species*
Amikacin *- Acinetobacter spp.*
Aztreonam *- E. coli, K. aerogenes, K. oxytoca, Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Enterobacter hormaechei, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, and Serratia marcescens*
Cefazolin *- K. pneumoniae*
Cefepime *- E. coli, K. aerogenes, K. oxytoca, K. pneumoniae, Citrobacter freundii, Enterobacter cloacae, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, and Serratia marcescens*
Ceftazidime *- E. coli, K. aerogenes, K. variicola, A. baumannii, P. aeruginosa, Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Enterobacter hormaechei, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, and Serratia marcescens*
Ceftazidime-avibactam *- K. aerogenes, K. oxytoca, Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Morganella morganii, Proteus mirabilis, and Serratia marcescens*
Ertapenem *- E. coli, K. aerogenes, K. oxytoca, K. pneumoniae, Citrobacter freundii, Enterobacter cloacae complex, Morganella morganii, and Serratia marcescens*
Gentamicin *- E. coli, K. pneumoniae, K. oxytoca, K. aerogenes, and Serratia marcescens*
Levofloxacin *- K. pneumoniae, K. oxytoca, K. aerogenes, Citrobacter freundii, Enterobacter cloacae complex, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, and Serratia marcescens*
Meropenem *- K. oxytoca, P. aeruginosa, Citrobacter koseri, Proteus mirabilis, Serratia marcescens*

Meropenem-vaborbactam *- K. pneumoniae, K. oxytoca, K. aerogenes, Citrobacter freundii, Enterobacter cloacae complex*
Piperacillin-tazobactam *– A.baumannii, K. pneumoniae, Citrobacter koseri, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, and Serratia marcescens*
Trimethoprim-sulfamethoxazole *- E. coli, K. aerogenes, K. variicola, and Proteus mirabilis*

The following drug/organism combinations showed low trending:

1. Ceftazidime-*M.morganii*
2. Meropenem-vaborbactam – *C.koseri and M.morganii*
3. Trimethoprim-*sulfamethoxazole-E.cloacae complex*

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

Ampicillin (AMP)

A total of 75 samples were evaluated with Ampicillin including 63 clinical (84.0%) and 12 challenge (16.0%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 98.7% and a CA of 100% with 0 VMJs (0.0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 55 *Proteus mirabilis* samples were evaluated with Ampicillin. The combined results from clinical and challenge testing demonstrated an EA of 98.2% and a CA of 100% with no VMJs (0%) and 0 MAJs (0%).
- A total of 20 *Salmonella spp.* samples were evaluated with Ampicillin. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Ampicillin with *Proteus mirabilis* and *Salmonella* spp. is acceptable.

Limitation(s)

N/A

Aztreonam (AZT)

A total of 365 samples were evaluated with Aztreonam including 290 clinical (79.5%) and 75 challenge (20.5%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 95.9% and a CA of 99.5% with 0 VMJs (0.0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 44 *Citrobacter freundii* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 95.5% and a CA of 100% with no VMJs (0%) and 0 MAJs (0%).

- A total of 66 *Citrobacter koseri* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 98.5% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

- A total of 42 *Enterobacter cloacae complex* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 97.6% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 41 *Morganella morganii* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 95.1% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 55 *Proteus mirabilis* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 92.7% and a CA of 98.2% with no VMJs (0%) and no MAJs (0%).
- A total of 28 *Proteus vulgaris* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 89.3% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 22 *Providencia rettgeri* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 95.2% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 14 *Providencia stuartii* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 53 *Serratia marcescens* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 98.1% and a CA of 98.1% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Aztreonam with *Enterobacter cloacae complex, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, and Serratia marcescens* is acceptable.

Limitation(s)

N/A

Cefepime (FEP)

A total of 299 samples were evaluated with Cefepime including 232 clinical (77.6%) and 67 challenge (22.4%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 96.7% and a CA of 98.0% with 0 VMJs (0.0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 44 *Citrobacter freundii* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 90.0% and a CA of 95.5% with no VMJs (0%) and 0 MAJs (0%).

- A total of 42 *Enterobacter cloacae complex* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 97.6% with no VMJs (0%) and no MAJs (0%).
- A total of 40 *Morganella morganii* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 92.5% and a CA of 92.5% with no VMJs (0%) and no MAJs (0%).
- A total of 55 *Proteus mirabilis* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 28 *Proteus vulgaris* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 22 *Providencia rettgeri* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 15 *Providencia stuartii* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

  A total of 53 *Serratia marcescens* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 94.3% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Cefepime with *Citrobacter freundii*, *Enterobacter cloacae, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, and Serratia marcescens* are acceptable.

Limitation(s)

N/A

Ceftazidime (TAZ)

A total of 346 samples were evaluated with Ceftazidime including 272 clinical (78.6%) and 74 challenge (21.4%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 94.5% and a CA of 97.1% with 1 VMJs (1.85%) and 0 MAJs (0.0%).

Species-level performance

- A total of 44 *Citrobacter freundii* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 90.9% and a CA of 100% with no VMJs (0%) and 0 MAJs (0%).
- A total of 68 *Citrobacter koseri* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 94.1% and a CA of 97.1% with no VMJs (0%) and no MAJs (0%).
- A total of 43 *Enterobacter cloacae complex* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 90.7% and a CA of 97.7% with 0 VMJs (0%) and no MAJs (0%).
- A total of 41 *Morganella morganii* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 95.1% and a CA of 95.1% with 1 VMJs (16.67%) and no MAJs (0%).
- A total of 55 *Proteus mirabilis* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 98.2% and a CA of 98.2% with no VMJs (0%) and no MAJs (0%).
- A total of 28 *Proteus vulgaris* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 14 *Providencia stuartii* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 92.9% and a CA of 92.9% with no VMJs (0%) and no MAJs (0%).
- A total of 53 *Serratia marcescens* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 94.3% and a CA of 94.3% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Ceftazidime with *Citrobacter freundii*, *Citrobacter koseri, Enterobacter cloacae complex, *Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, and Serratia marcescens* is acceptable.

**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.*

Limitation(s)

Perform an alternative method of testing prior to reporting results for the following organism(s):

- *Providencia rettgeri*

Ceftazidime-avibactam (AVI)

A total of 337 samples were evaluated with Ceftazidime-avibactam including 273 clinical (81.1%) and 64 challenge (18.9%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 98.5% and a CA of 100% with no VMJs (0. 0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 42 *Citrobacter freundii* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 95.2% and a CA of 100% with no VMJs (0%) and 0 MAJs (0%).
- A total of 67 *Citrobacter koseri* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 42 *Enterobacter cloacae complex* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 42 *Morganella morganii* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 54 *Proteus mirabilis* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 96.3% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 22 *Providencia rettgeri* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 15 *Providencia stuartii* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 53 *Serratia marcescens* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 98.1% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Ceftazidime-avibactam with *Citrobacter freundii*, *Citrobacter koseri, Enterobacter cloacae complex, Morganella morganii, Proteus mirabilis, Providencia rettgeri, Providencia stuartii, and Serratia marcescens* is acceptable.

Limitation(s)

N/A

Ertapenem (ETP)
A total of 278 samples were evaluated with Ertapenem including 224 clinical (80.6%) and 54 challenge (19.4%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 94.6% and a CA of 96.4% with no VMJs (0. 0%) and 2 MAJs (0.82%).

Species-level performance

- A total of 41 *Citrobacter freundii* samples were evaluated with Ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 90.2% and a CA of 95.1% with no VMJs (0%) and 1 MAJs (2.86%).
- A total of 68 *Citrobacter koseri* samples were evaluated with Ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 98.5% and a CA of 98.5% with no VMJs (0%) and no MAJs (0%).
- A total of 41 *Enterobacter cloacae complex* samples were evaluated with Ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 92.7% and a CA of 90.2% with no VMJs (0%) and **1 MAJs (3.45%).**
- A total of 39 *Morganella morganii* samples were evaluated with Ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 97.4% and a CA of 97.4% with no VMJs (0%) and no MAJs (0%).
- A total of 23 *Providencia rettgeri* samples were evaluated with Ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 15 *Providencia stuartii* samples were evaluated with Ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 51 *Serratia marcescens* samples were evaluated with Ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 90.2% and a CA of 96.1% with no VMJs (0%) and no MAJs (0%).

Conclusion
Performance for Ertapenem with *Citrobacter freundii*, *Citrobacter koseri, Enterobacter cloacae complex, Morganella morganii, Providencia stuartii, Providencia rettgeri, and Serratia marcescens* is acceptable.

Limitation(s)
Perform an alternative method of testing prior to reporting results for the following organism(s):

- *Proteus mirabilis*
- *Proteus vulgaris*
- *Enterobacter cloacae complex at MIC value of 2µg/mL due to the occurrence of 1 major error (1/29) susceptible isolates, (3.45%)*

Gentamicin (GEN)
A total of 206 samples were evaluated with Gentamicin including 166 clinical (80.6%) and 40 challenge (19.4%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 99.5% and a CA of 98.1% with 0 VMJs (0.0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 44 *Citrobacter freundii* samples were evaluated with Gentamicin. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 97.7% with no VMJs (0%) and 0 MAJs (0.0%).
- A total of 66 *Citrobacter koseri* samples were evaluated with Gentamicin. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 98.5% with no VMJs (0%) and no MAJs (0%).
- A total of 43 *Enterobacter cloacae complex* samples were evaluated with Gentamicin. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 53 *Serratia marcescens* samples were evaluated with Gentamicin. The combined results from clinical and challenge testing demonstrated an EA of 98.1% and a CA of 96.2% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Gentamicin with *Citrobacter freundii*, *Citrobacter koseri, Enterobacter cloacae, and Serratia marcescens* is acceptable.

Limitation(s)

Perform an alternative method of testing prior to reporting results for the following organism(s):

- *Proteus vulgaris*
- *Proteus mirabilis*

Levofloxacin (LEVO)

A total of 371 samples were evaluated with Levofloxacin including 285 clinical (76.8%) and 86 challenge (23.2%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 96.8% and a CA of 93.8% with 0 VMJs (0%) and 1 MAJs (0.35%).

Species-level performance

- A total of 44 *Citrobacter freundii* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 97.7% and a CA of 88.6% with no VMJs (0%) and 1 MAJs (2.86%).
- A total of 68 *Citrobacter koseri* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 98.5% and a CA of 97.1% with no VMJs (0%) and no MAJs (0%).
- A total of 50 *Enterobacter cloacae complex* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 94.0% and a CA of 90.0% with no VMJs (0%) and no MAJs (0%).

- A total of 41 *Morganella morganii* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 97.6% and a CA of 97.6% with no VMJs (0%) and no MAJs (0%).
- A total of 55 *Proteus mirabilis* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 90.9% and a CA of 96.4% with no VMJs (0%) and no MAJs (0%).
- A total of 29 *Proteus vulgaris* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 96.6% and a CA of 93.1% with no VMJs (0%) and no MAJs (0%).
- A total of 18 *Providencia rettgeri* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 88.9% with no VMJs (0%) and no MAJs (0%).
- A total of 13 *Providencia stuartii* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

  A total of 53 *Serratia marcescens* samples were evaluated with Levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 92.5% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Levofloxacin with *Citrobacter freundii*, *Citrobacter koseri, Enterobacter cloacae complex, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, and Serratia marcescens* is acceptable.

Limitation(s)

N/A

Meropenem (MERO)

A total of 261 samples were evaluated with Meropenem including 209 clinical (80.1%) and 52 challenge (19.9%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 94.3% and a CA of 98.5% with 0 VMJs (0.0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 44 *Citrobacter freundii* samples were evaluated with Meropenem. The combined results from clinical and challenge testing demonstrated an EA of 95.5% and a CA of 97.7% with no VMJs (0%) and 0 MAJs (0%).
- A total of 68 *Citrobacter koseri* samples were evaluated with Meropenem. The combined results from clinical and challenge testing demonstrated an EA of 94.1% and a CA of 98.5% with no VMJs (0%) and no MAJs (0%).

- A total of 41 *Enterobacter cloacae complex* samples were evaluated with Meropenem. The combined results from clinical and challenge testing demonstrated an EA of 92.7% and a CA of 97.6% with no VMJs (0%) and no MAJs (0%).
- A total of 53 *Proteus mirabilis* samples were evaluated with Meropenem. The combined results from clinical and challenge testing demonstrated an EA of 90.9% and a CA of 98.2% with no VMJs (0%) and no MAJs (0%).
- A total of 55 *Serratia marcescens* samples were evaluated with Meropenem. The combined results from clinical and challenge testing demonstrated an EA of 98.1% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Meropenem with *Citrobacter freundii*, *Citrobacter koseri, Enterobacter cloacae complex, Proteus mirabilis, and Serratia marcescens* is acceptable.

Limitation(s)

Perform an alternative method of testing prior to reporting results for the following organism(s):

- *Morganella morganii*
- *Proteus vulgaris*

Meropenem-vaborbactam (MEV)

A total of 339 samples were evaluated with Meropenem-vaborbactam including 274 clinical (80.8%) and 65 challenge (19.2%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 96.2% and a CA of 97.9% with no VMJs (0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 44 *Citrobacter freundii* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 93.2% and a CA of 97.7% with no VMJs (0%) and 0 MAJs (0%).
- A total of 68 *Citrobacter koseri* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 97.1% and a CA of 97.1% with no VMJs (0%) and no MAJs (0%).
- A total of 42 *Enterobacter cloacae complex* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 95.2% and a CA of 97.6% with no VMJs (0%) and no MAJs (0%).
- A total of 40 *Morganella morganii* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 95.0% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

- A total of 55 *Proteus mirabilis* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 94.5% and a CA of 96.4% with no VMJs (0%) and no MAJs (0%).
- A total of 22 *Providencia rettgeri* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 95.5% with no VMJs (0%) and no MAJs (0%).
- A total of 15 *Providencia stuartii* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 53 *Serratia marcescens* samples were evaluated with Meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Meropenem-vaborbactam with *Citrobacter freundii*, *Citrobacter koseri, Enterobacter cloacae, Morganella morganii, Proteus mirabilis, Providencia rettgeri, Providencia stuartii, and Serratia marcescens* is acceptable.

Limitation(s)

N/A

Piperacillin-tazobactam (P/T)

A total of 242 samples were evaluated with Piperacillin-tazobactam including 194 clinical (80.2%) and 48 challenge (19.8%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 95.9% and a CA of 94.6% with 0 VMJs (0.0%) and 3 MAJs (1.36%).

Species-level performance

- A total of 68 *Citrobacter koseri* samples were evaluated with Piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 94.1% and a CA of 91.2% with no VMJs (0.0%) and 1 MAJs (1.72%).
- A total of 55 *Proteus mirabilis* samples were evaluated with Piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 98.2% and a CA of 98.2% with no VMJs (0%) and 1 MAJs (1.89%).
- A total of 29 *Proteus vulgaris* samples were evaluated with Piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 96.6% and a CA of 96.6% with no VMJs (0%) and 1 MAJs (3.57%).

- A total of 22 *Providencia rettgeri* samples were evaluated with Piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 95.5% and a CA of 95.5% with no VMJs (0%) and no MAJs (0%).

- A total of 15 *Providencia stuartii* samples were evaluated with Piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 93.3% with no VMJs (0%) and no MAJs (0%).

- A total of 53 *Serratia marcescens* samples were evaluated with Piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 94.3% and a CA of 94.3% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Piperacillin-tazobactam with *Citrobacter koseri, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, and Serratia marcescens* is acceptable.

Limitation(s)

Perform an alternative method of testing prior to reporting results for the following organism(s):

- *Morganella morganii*
- *Proteus vulgaris at MIC value of 32µg/mL due to the occurrence of 1 major error (1/28) susceptible isolates, (3.57%)*

Trimethoprim-sulfamethoxazole (SXT)

A total of 165 samples were evaluated with Trimethoprim-sulfamethoxazole including 122 clinical (73.9%) and 43 challenge (26.1%) samples. The combined results from clinical and challenge testing from all claimed species demonstrated an EA of 98.8% and a CA of 99.4% with 0 VMJs (0.0%) and 0 MAJs (0.0%).

Species-level performance

- A total of 43 *Enterobacter cloacae* samples were evaluated with Trimethoprim-sulfamethoxazole. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 54 *Proteus mirabilis* samples were evaluated with Trimethoprim-sulfamethoxazole. The combined results from clinical and challenge testing demonstrated an EA of 100% and a CA of 100% with no VMJs (0%) and no MAJs (0%).
- A total of 28 *Proteus vulgaris* samples were evaluated with Trimethoprim-sulfamethoxazole. The combined results from clinical and challenge testing demonstrated an EA of 96.4% and a CA of 96.4% with no VMJs (0%) and no MAJs (0%).

Conclusion

Performance for Trimethoprim-sulfamethoxazole with *Enterobacter cloacae, Proteus mirabilis, Proteus vulgaris,* is acceptable.

Limitation(s)

N/A

Quality Control

Strains recommended by the FDA and CLSI and the LifeScale QC strain (*Enterobacter cloacae* ABGNQC1) were tested for each antimicrobial agent evaluated using the LifeScale AST System LSGN Panel and the CLSI Reference Broth Microdilution Method. The quality control (QC) strains tested were *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 700603, and *Enterobacter cloacae* ABGNQC1. The QC testing results for all antimicrobics on the LSGN panel are detailed in Tables 5-17.

QC <95% explanation: The observed QC errors could be associated with the frequency of subculturing which may cause a decline in viability leading to inconsistent performance. In all cases where QC were out of range, the subsequent repeat tests, performed with a fresh subculture were within range indicating that the system was functioning properly and the initial failures were not systemic. MCW and LACNY experienced sporadic QC outliers for Meropenem and Gentamicin. Overall, these findings reflect isolated occurrences tied to organism, rather than systemic issues with the LifeScale system or test performance.
In the previous submission K241324, LifeScale demonstrated robust QC performance with Meropenem achieving >98% within range results and Gentamicin at 100%. The few recent QC outliers observed were isolated and linked issues with strain integrity.
To prevent recurrence for future studies all sites will be reminded to follow subculturing schedules per the protocol, and QC organism handling procedures.

Amikacin

QC Organism	Expected Range (µg/mL)	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
	8 – 32	<=4				

Enterobacter cloacae ABGNQC1		**8**		9	2	2
		16	18	15	23	17
		32	10		7	4
		64			1	
		128				
		256				
		>256				
Total			**28/28 (100%)**	**24/24 (100%)**	**32/33 (97.0%)**	**23/23 (100%)**

Table 5. LifeScale AST System QC MIC Distribution for Amikacin

Ampicillin

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
Escherichia coli ATCC 25922	<=2-8	**<=2**	4	21	22	18
		4	24	6	9	6
		8	1			
		16				
		32				
		64				
		>64				
Total			**29/29 (100%)**	**27/27 (100%)**	**31/31 (100%)**	**24/24 (100%)**

Table 6. LifeScale AST System QC MIC Distribution for Ampicillin

Aztreonam

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	[a] **Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
Pseudomonas aeruginosa ATCC 27853	2-8	<=1	2			
		2	4	20	26	24
		4	25	3	6	1
		8	5	1	1	
		16				
		32				

		64				1
		>64				
Total			**34/36 (94.4%)**	**24/24 (100%)**	**33/33 (100%)**	**25/26 (96.2%)**

Table 7. LifeScale AST System QC MIC Distribution for Aztreonam

Cefazolin

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
Escherichia coli ATCC 25922	1-4	<=0.25				
		0.5				
		1	2			
		2	27	23	26	21
		4		4	4	3
		8				
		16				
		>16			1	
Total			**29/29 (100%)**	**27/27 (100%)**	**30/31 (96.8%)**	**24/24 (100%)**

Table 8. LifeScale AST System QC MIC Distribution for Cefazolin

Cefepime

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**

Pseudomonas aeruginosa ATCC 27853	0.5-4	**<=0.5**	6	2		
		1	24	7	23	16
		2	6	14	7	9
		4		1	1	1
		8				
		16				
		32				
		64				
		>64				
Total			**36/36 (100%)**	**24/24 (100%)**	**31/31 (100%)**	**26/26 (100%)**

Table 9. LifeScale AST System QC MIC Distribution for Cefepime

Ceftazidime

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
K. pneumoniae ATCC 700603	16-64	<=1				
		2				
		4				
		8				
		16		25	28	22
		32	20		2	
		64	10			
		>64				
Total			**30/30 (100%)**	**25/25 (100%)**	**30/30 (100%)**	**22/22 (100%)**

Table 10. LifeScale AST System QC MIC Distribution for Ceftazidime

Ceftazidime-avibactam

QC Organism	**Expected Range**	Conc. µg/mL	Reference Frequency	New Device Test Frequency

	(µg/mL)	Sites →	Ref Lab (ABIO)	ABIO	LACNY	MCW
Enterobacter cloacae ABGNQC1	<=2/4-8/4	**<=2/4**	11		5	4
		4/4	17	8	27	16
		8/4		16	1	2
		16/4				1
		32/4				
		>32/4				
Total			**28/28 (100%)**	**24/24 (100%)**	**33/33 (100%)**	**22/23 (95.7%)**

Table 11. LifeScale AST System QC MIC Distribution for Ceftazidime-avibactam

Ertapenem

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	[a] **Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
Pseudomonas aeruginosa ATCC 27853	2-8	<=0.12				
		0.25				
		0.5				
		1	3			
		2	20	13	27	13
		4	8	9	6	13
		8	5	2		
		>8				
Total			**33/36 (92.0%)**	**24/24 (100%)**	**33/33 (100%)**	**26/26 (100%)**

Table 12. LifeScale AST System QC MIC Distribution for Ertapenem

Gentamicin

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	[a] **Ref Lab (ABIO)**	**ABIO**	[a] **LACNY**	[a] **MCW**

Enterobacter cloacae ABGNQC1	8-32	<=1				
		2				
		4				
		8				
		16	20	23	18	14
		32	6	1	12	7
		>32	2		3	2
Total			**26/28 (93.0%)**	**24/24 (100%)**	**30/33 (91.0%)**	**21/23 (91.3%)**

Table 13. LifeScale AST System QC MIC Distribution for Gentamicin

Levofloxacin

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	[a] **Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
Pseudomonas aeruginosa ATCC 27853	0.5-4	<=0.25	3			
		0.5	21	23	31	12
		1	12	1		14
		2				
		4				
		8				
		16				
		>16				
Total			**33/36 (92.0%)**	**24/24 (100%)**	**31/31 (100%)**	**26/26 (100%)**

Table 14. LifeScale AST System QC MIC Distribution for Levofloxacin

Meropenem

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	[a] **LACNY**	[a] **MCW**
	<=0.12-1	**<=0.12**	6			

Pseudomonas aeruginosa ATCC 27853		**0.25**	25	20	20	9
		0.5	5	2	6	9
		1		1	1	4
		2		1	2	
		4				2
		8				2
		16			2	
		>16				
Total			**36/36 (100%)**	**23/24 (95.8%)**	**27/31 (87.1%)**	**22/26 (84.6%)**

Table 15. LifeScale AST System QC MIC Distribution for Meropenem

Meropenem-vaborbactam

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
Enterobacter cloacae ABGNQC1	4/8-16/8	<=0.5/8				
		1/8				
		2/8				
		4/8	12			
		8/8	16	14	22	13
		16/8		10	11	10
		>16/8				
Total			**28/28 (100%)**	**24/24 (100%)**	**33/33 (100%)**	**23/23 (100%)**

Table 16. LifeScale AST System QC MIC Distribution for Meropenem-vaborbactam

Piperacillin-tazobactam

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
	8/4-32/4	<=4/4				

K. pneumoniae ATCC 700603		**8/4**		25	28	22
		16/4	29		2	
		32/4	1			
		64/4				
		128/4				
		256/4				
		>256/4				
Total			**30/30 (100%)**	**25/25 (100%)**	**30/30 (100%)**	**22/22 (100%)**

Table 17. LifeScale AST System QC MIC Distribution for Piperacillin-tazobactam

Trimethoprim-sulfamethoxazole

QC Organism	**Expected Range (µg/mL)**	Conc. µg/mL	Reference Frequency	New Device Test Frequency		
		Sites →	**Ref Lab (ABIO)**	**ABIO**	**LACNY**	**MCW**
Pseudomonas aeruginosa ATCC 27853	<=0.5	**<=0.25**	29	27	31	24
		0.5				
		1				
		2				
		4				
		8				
		>8				
Total			**29/29 (100%)**	**27/27 (100%)**	**31/31 (100%)**	**24/24 (100%)**

Table 18. LifeScale AST System QC MIC Distribution for Trimethoprim-sulfamethoxazole

[a] All out of range QC results were repeated with fresh subculture and were within expected range. Results are considered acceptable.

Removal of limitations included in K211815/K241234

Additional clinical evaluation testing was performed to support the removal of limitations and updated breakpoints included in the cleared LifeScale LSGN Kit with the LifeScale AST system (K211815/K241324), Ceftazidime-avibactam, and Aztreonam (limitation revision/removal) and Cefepime, Ceftazidime and Piperacillin-tazobactam (updated breakpoints).

Total Evaluated	No. EA	EA%	Eval Tot	No. Eval EA	Eval EA%	No. CA	CA%	No. R	No. S	#MIN (MIN%)	#MAJ (MAJ%)	#VMJ (VMJ%)
Ceftazidime-avibactam - *K. pneumoniae* [Breakpoints (µg/mL): ≤8/4 (S), ≥16/4 (R)]												
173	**171**	**98.8%**	**9**	**7**	**77.8%**	**170**	**98.3%**	**50**	**123**	**N/A**	**1 (0.81%)**	**1 (2.00%)**
Aztreonam-*P.aeruginosa* [Breakpoints (µg/mL): ≤8 (s), 16 (I),≥32 (R)]												
185	**178**	**96.2%**	**129**	**122**	**94.6%**	**168**	**90.8%**	**101**	**73**	**14 (7.57%)**	**1 (1.37%)**	**2 (1.98%)**
Cefepime-*P.aeruginosa* [Breakpoints (µg/mL): ≤4 (s), 8 (I),≥16 (R)]												
101	**94**	**93.1%**	**78**	**71**	**91.0%**	**81**	**80.2%**	**21**	**72**	**18.81%**	**0 (0.00%)**	**1 (4.76%)**
Ceftazidime-*P.aeruginosa* [Breakpoints (µg/mL): ≤8 (s), 16 (I),≥32 (R)]												
116	**107**	**92.2%**	**85**	**76**	**89.4%**	**104**	**89.7%**	**52**	**61**	**9.48%**	**0 (0.00%)**	**1 (1.92%)**
Piperacillin-tazobactam-*P.aeruginosa* [Breakpoints (µg/mL): ≤16/4 (s), 32/4 (I),≥64/4 (R)]												
185	**174**	**94.1%**	**59**	**48**	**81.4%**	**172**	**93.0%**	**60**	**118**	**5.95%**	**1 (0.85%)**	**1 (1.67%)**

Table 19. LifeScale LSGN performance for the removal of limitations and updated breakpoints included in K211815/K241324: Interpretation of MIC results are based on FDA Susceptibility Test Interpretative Criteria (STIC) and the 34th edition of the CLSI M100

Summary of Results for Limitation Removal and Updated Breakpoints

Ceftazidime-avibactam/*K. pneumoniae*

Based on the original data provided a total of 142 *K. pneumoniae* samples were evaluated with Ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 98.6% and a CA of 98.6% with 1 VMJs (5.00%) and 1 MAJs (0.82%). Due to the high VMJ rate the following limitation is proposed:

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

To resolve the noted limitation, additional clinical testing was conducted for Ceftazidime-avibactam and *K.pneumoniae*. A total of 31 additional *K. pneumoniae* samples were added to the original Ceftazidime-avibactam clinical data submitted in K211815 and K241324 for a total of 173 isolates. The combined results from clinical and challenge testing demonstrated an EA of 98.8% and a CA of 98.3% with 1VMJ error (2.00%) and 1 MAJ errors (0.81%).

Aztreonam/*P. aeruginosa*

Based on the original data provided a total of 116 *P.aeruginosa* samples were evaluated with Aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 94.0% and a CA of 87.9% with 2 VMJs (3.70%) and 1 MAJs (1.85%). Due to the high VMJ rate the following limitation is proposed:

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

To resolve the noted limitation, additional clinical testing was conducted for Aztreonam and *P.aeruginosa*. A total of 69 Additional *P.aeruginosa* samples were added to the original Aztreonam clinical data submitted in K211815 for a total of 185 isolates. The combined results from clinical and challenge testing demonstrated an EA of 96.2% and a CA of 90.8% with 2 VMJ errors (1.98%) and 1 MAJ errors (1.37%).

Update Breakpoints

Cefepime/*P. aeruginosa*

Based on the original data a total of 101 *P. aeruginosa* samples were evaluated with Cefepime. The combined results from clinical and challenge testing demonstrated an EA of 93.1% and a CA of 84.2% with 3 VMJs (10.34%) and 13 MAJ (18.06%). Due to the lack of an intermediate breakpoint the MAJ rate can be adjusted to 2.78% since 11/13 MAJ discrepancies were in essential agreement to the

reference method. Due to the high VMJ error rate at 4 µg/mL the following limitation was proposed:

For Cefepime, perform an alternative method of testing prior to reporting of results for P. aeruginosa when the MIC is 4 µg/mL due to the occurrence of very major errors (3/29 resistant isolates, 10.34%). ***Cefepime****: P. aeruginosa when the MIC is 4 µg/mL due to the occurrence of very major errors (1/21 resistant isolates, 4.7%).*

With the updated breakpoints, the combined results from clinical and challenge testing demonstrated acceptable performance with an EA of 93.1%, EA evaluable of 91.0% and a CA of 80.2% with 1 VMJ error (4.7%) and 0 MAJ errors (0.0%).

These data support the modification to the limitation, as the revised breakpoints more accurately reflect current clinical interpretive criteria and provide improved alignment between the test system and the reference method. The limitation was updated to reflect the validated performance under these revised breakpoints

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

Cefepime*: P. aeruginosa when the MIC is 4 µg/mL due to the occurrence of very major errors (1/21 resistant isolates, 4.7%).*

Ceftazidime/*P. aeruginosa*

Based on the original data A total of 116 *P. aeruginosa* samples were evaluated with Ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 92.2% and a CA of 94.0% with two VMJs (3.64%) and five MAJ (8.20%). Due to lack of an intermediate breakpoint, one VMJ was in Essential agreement bringing the adjusted VMJ rate to 1.82%. Perform an alternative method of testing prior to reporting results for:

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 a lack of an intermediate breakpoint).

With the updated breakpoints, the combined results from clinical and challenge testing demonstrated acceptable performance with an EA of 92.2% and a CA of 89.7% with 1 VMJ error (1.92%) and 0 MAJ errors (0.0%).

These results meet the predefined performance acceptance criteria and support removal of the prior limitation. The limitation was therefore removed from the labeling, as the updated breakpoints adequately address the previous performance concern and the device demonstrated consistent and reliable performance under the revised interpretive criteria.

Piperacillin-tazobactam/*P. aeruginosa*

A total of 185 *P. aeruginosa* samples were evaluated with Piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 94.1% and a CA of 93.5% with 1 VMJ (1.49%) and 1 MAJ (0.89%).

With the updated breakpoints, the combined results from clinical and challenge testing demonstrated acceptable performance with an EA of 94.1% and a CA of 93.0% with 1 VMJ error (1.67%) and 1 MAJ errors (0.85%).

7. Analytical Performance Data

New Blood Bottle Equivalency Study

LifeScale LSGN Blood Bottle Compatibility

Organisms tested: 14

- *Escherichia coli (5)*
- *Klebsiella pneumoniae (5)*
- *Acinetobacter baumannii (2)*
- *Pseudomonas aeruginosa (2)*

New Blood Bottles Tested:

- BD BACTEC™ Plus Anaerobic
- BacT/ALERT® FA Plus Aerobic
- BacT/ALERT® FN Plus Anaerobic

Reference Blood Bottle Tested

- BD BACTEC™ Standard Aerobic

The objective of this study was to assess the compatibility of the LifeScale AST system with various commonly used blood culture bottle types. Three blood culture bottle types from two different blood culture manufacturers Becton Dickinson (BD BACTEC™ Plus Anaerobic), and bioMérieux, inc. BacT/ALERT® FA Plus Aerobic, BacT/ALERT® FN Plus Anaerobic) were evaluated analytically with the LifeScale LSGN AST system. Ten replicates of each positive blood culture were tested using
the LifeScale LSGN kit within 12 hours of positivity. Results from each media were compared to the modal MIC (Minimal Inhibitory Concentration) of the BD BACTEC™ Standard Aerobic Bottle LifeScale AST results.

Results and Discussion

The performance of each additional blood bottle was evaluated for Amikacin, Ampicillin, Aztreonam, Cefazolin, Cefepime, Ceftazidime, Ceftazidime-avibactam, Ertapenem, Gentamicin, Levofloxacin, Meropenem, Meropenem-vaborbactam, Piperacillin-tazobactam and Trimethoprim-sulfamethoxazole.

Evaluable results were targeted for each antimicrobial/organism to prove equivalence. Line data is available for each antimicrobial/organism combination with evaluated and non-evaluated results.

Conclusion

Amikacin, Ampicillin, Aztreonam, Cefazolin, Cefepime, Ceftazidime, Ceftazidime-avibactam, Ertapenem, Gentamicin, Levofloxacin, Meropenem, Meropenem-vaborbactam, Piperacillin-tazobactam and Trimethoprim-sulfamethoxazole were assessed for their susceptibility testing against various bacterial strains across different blood bottle types and aerobic/anaerobic conditions. Results for most drug/organism combinations for claimed species showed good performance with all blood culture bottles with the following exceptions:

- *A. baumannii* with Amikacin when tested using the following blood culture bottle type: bioMérieux FA Plus Aerobic

- *Escherichia coli* with Meropenem-vaborbactam when tested using the following blood culture bottle types: bioMérieux FA Plus Aerobic, FN Plus Anaerobic and BD BACTEC Plus Anaerobic.

Overall, the study suggests that these antibiotics can effectively assess the susceptibility of bacterial strains in blood cultures, but there may be variations in performance depending on the specific antibiotic, bacterial strain, and blood bottle type used resulting in potential limitations or footnotes.