510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K230675

B Applicant

Specific Diagnostics, LLC

C Proprietary and Established Names

VITEK REVEAL GN AST Assay and VITEK REVEAL 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 Testing	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 substantial equivalence determination for use of the VITEK REVEAL AST System and VITEK REVEAL GN AST Assay for testing positive blood culture samples to determine the minimum inhibitory concentration of specific antimicrobials with specific Gram-negative organisms.

B Measurand:

Antimicrobial	Reporting Range
Amikacin	≤0.5 to >128 µg/mL
Amoxicillin/clavulanate	≤2/1 to >64/32 µg/mL
Ampicillin/sulbactam	≤2/1 to >64/32 µg/mL
Aztreonam	≤0.25 to >64 µg/mL
Cefepime	≤0.125 to >64 µg/mL
Cefotaxime	≤0.25 to >128 µg/mL
Ceftazidime	≤0.125 to >64 µg/mL
Ceftazidime/Avibactam	≤0.0625/4 to >32/4 µg/mL
Ceftolozane/Tazobactam	≤0.0625/4 to >32/4 µg/mL
Ceftriaxone	≤0.25 to >16 µg/mL
Cefuroxime	≤1 to >32 µg/mL
Ciprofloxacin	≤0.0625 to >8 µg/mL
Ertapenem	≤0.125 to >16 µg/mL
Gentamicin	≤0.25 to >32 µg/mL
Imipenem	≤0.25 to >16 µg/mL
Levofloxacin	≤0.125 to >16 µg/mL
Meropenem	≤0.0625 to >32 µg/mL
Meropenem/Vaborbactam	≤0.0625/8 to >32/8 µg/mL
Piperacillin/Tazobactam	≤2/4 to >256/4 µg/mL
Tetracycline	≤1 to >64 µg/mL
Tobramycin	≤0.125 to >32 µg/mL
Trimethoprim/Sulfamethoxazole	≤0.5/9.5 to >64/1216 µg/mL
ESBL	POS/NEG

C Type of Test:
Quantitative and qualitative antimicrobial susceptibility test (AST) system that utilizes sensors to detect metabolic byproducts of microbial growth from positive blood culture samples to determine the minimum inhibitory concentration (MIC) of specific antimicrobial-organism combinations.

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use.

B Indication(s) for Use:
The VITEK REVEAL AST System is an automated system for quantitative and qualitative antimicrobial susceptibility testing (AST) of organisms direct from positive blood culture. The VITEK REVEAL AST System does not provide organism identification.

The VITEK REVEAL AST System is an automated system that uses an array of sensors to detect volatile organic compounds emitted by growing bacteria for the *in vitro* quantitative and qualitative determination of antimicrobial susceptibility. The VITEK REVEAL GN AST Assay is indicated for susceptibility testing direct from positive blood culture samples signaled as positive by a continuous monitoring blood culture system and confirmed to contain gram-

negative bacilli by Gram stain. Organism identification is required for AST result interpretation and reporting.

This test is performed by laboratory health professionals in a clinical diagnostic setting. Results may be used as an aid to clinicians in determining appropriate antimicrobial therapy. Test results from the VITEK REVEAL AST System should be interpreted 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. Sub-culturing is necessary to support further testing for: bacteria and antimicrobials not on the VITEK REVEAL GN AST Assay panel, inconclusive results, epidemiologic testing, recovery of organisms present in positive blood cultures samples, and susceptibility testing of bacteria in polymicrobial samples.

The VITEK REVEAL GN AST Assay tests the following antimicrobial agents with the specific target organisms identified below:

Amikacin: *Acinetobacter baumannii-calcoaceticus* complex, *Citrobacter freundii* (including *Citrobacter freundii* complex), *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Serratia marcescens*

Amoxicillin/clavulanate: *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group, *Proteus mirabilis*

Ampicillin/sulbactam: *Escherichia coli*, *Klebsiella oxytoca*, *Proteus mirabilis*

Aztreonam: *Citrobacter freundii* (including *C. freundii* complex), *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Pseudomonas aeruginosa*

Cefepime: *Citrobacter koseri* (syn. *C. diversus*), *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella* species (including *K. pneumoniae* group and *K. aerogenes*), *Klebsiella oxytoca*, *Pseudomonas aeruginosa*

Cefotaxime: *Acinetobacter baumannii-calcoaceticus* complex, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group

Ceftazidime: *Acinetobacter baumannii-calcoaceticus* complex, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group

Ceftazidime/avibactam: *Citrobacter freundii* complex, *Citrobacter koseri*, *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus mirabilis*, *Pseudomonas aeruginosa*

Ceftolozane/tazobactam: *Citrobacter koseri*, *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*

Ceftriaxone: *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus mirabilis*

Cefuroxime: *Citrobacter koseri*, *Escherichia coli*, *Klebsiella pneumoniae* group, *Klebsiella oxytoca*, *Proteus mirabilis*

Ciprofloxacin: *Citrobacter freundii* (including *C. freundii* complex), *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Serratia marcescens*

Ertapenem: *Escherichia coli*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus mirabilis*, *Proteus vulgaris*

Gentamicin: *Citrobacter freundii* complex, *Citrobacter koseri*, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Serratia marcescens*

Imipenem: *Acinetobacter baumannii-calcoaceticus* complex, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group, *Pseudomonas aeruginosa*, *Serratia marcescens*

Levofloxacin: *Citrobacter koseri*, *Citrobacter freundii* (including *C. freundii* complex), *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Serratia marcescens*

Meropenem: *Acinetobacter baumannii-calcoaceticus* complex, *Enterobacter cloacae* (including *E. cloacae* complex), *Escherichia coli*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Serratia marcescens*

Meropenem/vaborbactam: *Citrobacter freundii* (incluidng *C. freundii* complex), *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus mirabilis*

Piperacillin/tazobactam: *Citrobacter koseri*, *Escherichia coli*, *Klebsiella pneumoniae* (including *K. pneumoniae* group), *Proteus vulgaris*

Tetracycline: *Acinetobacter baumannii-calcoaceticus* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group

Tobramycin: *Citrobacter freundii* complex, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Serratia marcescens*

Trimethoprim/sulfamethoxazole: *Escherichia coli*, *Klebsiella aerogenes*, *Klebsiella pneumoniae* group

ESBL Confirmation test: *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae* group

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

The VITEK REVEAL GN AST Assay can only be used with the VITEK REVEAL AST System.

The VITEK REVEAL GN AST Assay should not be used for any clinical specimens other than monomicrobial positive blood cultures containing Gram-negative bacteria.

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

Positive blood cultures should be tested immediately after a positive flag, where possible. A 16-hour sample stability claim is included in case of instrument errors or if re-testing is needed.

The performance of the VITEK REVEAL AST Assay has only been evaluated using the following blood culture bottles:
BD BACTEC Plus Aerobic
BD BACTEC Plus Anaerobic
BD BACTEC Standard Aerobic
BD BACTEC Standard Anaerobic
BD BACTEC Lytic Anaerobic
BD BACTEC Peds Plus
bioMérieux BACT/ALERT FA Plus
bioMérieux BACT/ALERT FN Plus
bioMérieux BACT/ALERT PF Plus
bioMérieux BACT/ALERT SA
bioMérieux BACT/ALERT SN

The following limitations were added to the device labeling based on performance demonstrated in the current submission:

For amikacin, perform an alternative method of testing prior to reporting of results for *A. baumannii-calcoaceticus* complex when the MIC is 32 µg/mL due to the occurrence of minor errors, that were in essential agreement, resulting in a category agreement below 90%.

For amoxicillin/clavulanate, perform an alternative method of testing prior to reporting of results for *E. coli* when the MIC is 16 µg/mL due to the occurrence of minor errors, that were in essential agreement, resulting in a category agreement below 90%.

Due to the occurrence of a major errors with cefuroxime, isolates of *K. pneumoniae* group that provide a MIC of 16 µg/mL should be retested by an alternate method.

Due to the occurrence of a major errors with cefuroxime, isolates of *K. oxytoca* that provide a MIC of 32 µg/mL should be retested by an alternate method.

Due to the occurrence of a major error with cefuroxime, isolates of *C. koseri* that provide a MIC of > 32 µg/mL should be retested by an alternate method.

Due to the occurrence of a very major error with ciprofloxacin, isolates of *P. mirabilis* that provide a MIC of 0.25 µg/mL should be retested by an alternate method.

Due to the occurrence of a very major error with gentamicin, isolates of *E. coli* that provide a MIC of 4 µg/mL should be retested by an alternate method.

Due to the occurrence of very major errors with imipenem, isolates of *P. aeruginosa* that provide a MIC of 2 µg/mL should be retested by an alternate method.

Due to the occurrence of a very major error with levofloxacin, isolates of *P. mirabilis* that provide a MIC of 0.5 µg/mL should be retested by an alternate method.

Due to the occurrence of a very major error with piperacillin/tazobactam, isolates of *E. coli* that provide a MIC of 8 µg/mL should be retested by an alternate method.

Due to the occurrence of very major errors with tobramycin, isolates of *E. coli* that provide a MIC of 4 µg/mL should be retested by an alternate method.

Tobramycin with *S. marcescens* may produce a resistant result that can be found susceptible by the reference method. If critical to patient care, confirm these results with an alternate method.

Due to the occurrence of major error with Trimethoprim/sulfamethoxazole, isolates of *E. coli* that provide a MIC of 4-64 µg/mL should be retested by an alternate method.

Isolates of *K. oxytoca* that test as ESBL positive should be retested by an alternate method to confirm the presence of ESBL.

Interference has not been established for the following drug/organism combination for all interferents, except platelets: amoxicillin-clavulanate/Enterobacterales, aztreonam/Enterobacterales, cefepime/Enterobacterales, ceftazidime/Enterobacterales, ceftriaxone/Enterobacterales, ciprofloxacin/*P. aeruginosa*, levofloxacin/*P. aeruginosa*, ertapenem/Enterobacterales, imipenem/Enterobacterales.

During clinical studies, it was observed that mishandling of the sealed plates may cause the sample to wet the sensor. This may result in abnormal sensor responses contributing to inaccurate growth detection.

D Special Instrument Requirements:
VITEK REVEAL GN AST Assay must be used with the VITEK REVEAL AST System, Software Version 1.2.5 or higher.

IV Device/System Characteristics:

A Device Description:
The VITEK REVEAL AST System is an *in vitro* diagnostic (IVD) automated platform for phenotypic Antimicrobial Susceptibility Testing (AST) of bacterial samples, directly from positive blood cultures. The System utilizes growth-based broth microdilution (BMD) principles to rapidly determine Minimum Inhibitory Concentrations (MIC) for the drugs on the VITEK REVEAL GN AST Assay. In combination with species identification (obtained from an FDA-cleared rapid bacterial identification method), the system will provide a Susceptible /

Intermediate / Resistant ("SIR") and/or extended-spectrum β-lactamase (ESBL) determination for the species tested. The VITEK REVEAL AST System is indicated for susceptibility testing of specific pathogenic bacteria commonly associated with bacteremia.

The VITEK REVEAL AST System detects bacterial growth using an array of chemical Small Molecule Sensors (SMS), which change color in the presence of various metabolic gases (VOC; volatile organic compounds) emitted by growing bacteria during incubation. The SMS arrays, printed onto a VITEK REVEAL Sensor Panel, are positioned atop each well of an inoculated VITEK REVEAL Antibiotic Panel in an AST disposable assembly comprising a VITEK REVEAL GN AST Assay.

There are four key components unique to the VITEK REVEAL AST System: 1) VITEK REVEAL Antibiotic Panels; 2) VITEK REVEAL Sensor Panel; 3) VITEK REVEAL Sealer; 4) VITEK REVEAL Instrument. In addition, the provided inoculator is required for inoculation of the VITEK REVEAL Antibiotic Panels.

Reporting of VITEK REVEAL AST results requires a species identification, which can be obtained by using an FDA-cleared bacterial identification method.

B Principle of Operation:

The VITEK REVEAL sensor technology is based on novel, proprietary chemical Small Molecule Sensors (SMS) that sensitively register a "fingerprint" of complex volatile compound mixtures. The sensors comprising the array have distinct chemical reactivity with volatiles and changes color upon exposure to low concentrations of volatile organic compounds (VOCs) emitted by populations of microorganisms during growth.

The VITEK REVEAL AST System leverages this sensitive capability to detect growth, using an array of seven sensors positioned over each well of a 96-well antibiotic panel. Thus, the VITEK REVEAL Sensor Panels consist of a sheet of 96, 7-sensor arrays heat-sealed to a 96-well Antibiotic Panel so that when inoculated with bacteria, each array individually responds to the volatiles emitted in that well to sensitively register growth.

Bacterial growth or inhibition in each antimicrobial-containing well is determined by the VITEK REVEAL AST System based on the change in color intensity of the corresponding SMS array compared to the sensor responses in the positive control (no antimicrobials) and negative control (no growth media) wells. An algorithm detects the divergence between the compared SMS responses and rapidly determines growth (indicating resistance) or inhibition (indicating susceptibility) for each two-fold doubling dilution of each antimicrobial thereby enabling a quantitative MIC determination directly analogous to BMD. Once the identification (ID) using a result of an FDA-cleared method is furnished to the system, the MIC result enables the system to generate an interpretation (SIR/ESBL result) based on the FDA-recognized breakpoints. MICs and interpretations are displayed only after the species ID has been entered into the system.

C Instrument Description Information:

1. Instrument Name:
   VITEK REVEAL AST System

2. Specimen Identification:
   The user enters sample information into the user interface or sample information is transferred to the VITEK REVEAL system via an LIS connection. To ensure sample traceability, the user prints a sample barcode label and places the barcode label on the area of the Sensor Panel where indicated. The sample barcode encodes the sample ID and associated information. There is a separate sensor barcode which encodes the sensor/array information.

3. Specimen Sampling and Handling:
   The workflow requires an aliquot from a positive blood culture sample that has been confirmed to be Gram-negative and monomicrobial by a Gram stain. The aliquot is diluted into a tube of Pluronic water and the Pluronic suspension is poured into the provided inoculator tray. The provided inoculator is used to dispense the suspension into each well of the 96-well VITEK REVEAL Antibiotic Panel. A VITEK REVEAL Sensor Panel is then placed onto the Antibiotic Panel, and the VITEK REVEAL Sealer seals the Sensor Panel onto the Antibiotic Panel such that an array of seven (7) sensors is positioned over each well. The sealed Antibiotic Panel is then loaded on the VITEK REVEAL Instrument. The VITEK REVEAL Instrument will automatically begin the run. Any time after the run has started, the species ID may be entered into the system. The MIC determinations and SIR/ESBL interpretations are visible on the user interface.

4. Calibration:
   The VITEK REVEAL Instrument and software has the following internal Quality Control (QC) checks:

   - VITEK REVEAL Instrument drawer incubation temperature has low and high limits that, when exceeded, will display alarms on the user interface.
   - Should either the sensor barcode or sample barcode be unreadable, a default artificial barcode would be assigned, using the instrument ID, plate location, and the current timestamp. An alert will be displayed on the user interface, and the user will have the option to enter the information manually.
   - If the instrument does not identify or cannot locate the 96 well plate, an alert is provided to the user to examine the plate to confirm it is placed correctly in the instrument.
   - If the initial intensity of a sensor is above a certain threshold, it suggests poor quality of the sensor and the user is alerted to retest the sample using a sensor from a new lot. If sensor quality is affected only in certain wells, then the result for the affected antibiotic alone will be suppressed.
   - If there is insufficient growth in the positive control well, then no results are reported, the user is alerted to the possibility of insufficient inoculum or a slow growing organism, and the user is advised to retest the sample.
   - If there is growth detected in the negative control well, then a warning message is displayed on the user interface to alert the user.
   - Each VOC sensor has a QC check to ensure that the sensor quality is acceptable. If a particular sensor fails this check in any well, then that sensor is not used.

5. Quality Control:
   In addition to the above controls, QC testing of the VITEK REVEAL Instrument and the Sealer should be performed as dictated by the laboratory's protocols. The purpose of external Quality Control (QC) testing is to monitor performance of the VITEK REVEAL AST

System (including the Sensor Panels and Antibiotic Panels) and the VITEK REVEAL Sealer, as well as the proficiency of the laboratory personnel who use the system.

VITEK REVEAL AST System QC is performed by testing the manufacturer recommended QC strains. The QC workflow follows the same steps as the sample workflow, with the exception that provided QC sample barcodes are placed on the GN AST assay, which automatically instructs the instrument to operate in QC mode. The QC results are generated and displayed on the user interface indicating the expected QC MIC range, the VITEK REVEAL MIC call, and whether the relevant antimicrobials for the organism have passed or failed. See more details about quality control in section VII.A. below.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Accelerate Pheno system, Accelerate Phenotest BC Kit

B Predicate 510(k) Number(s):
K192665

C Comparison with Predicate(s):

Device & Predicate Device(s):	**VITEK REVEAL AST System and VITEK REVEAL GN AST Assay K230675**	**Accelerate Pheno System and PhenoTest BC Kit K192665**
Device Trade Name	VITEK REVEAL GN AST Assay and VITEK REVEAL AST System	Accelerate Pheno System and PhenoTest BC Kit
General Device Characteristic Similarities		
Intended Use/Indications For Use	The VITEK REVEAL AST System is an *in vitro* diagnostic (IVD) automated system for quantitative and qualitative antimicrobial susceptibility testing (AST) of organisms direct from positive blood culture. The VITEK REVEAL AST System does not provide organism identification.	The Accelerate PhenoTest BC kit is a multiplexed *in vitro* diagnostic test utilizing both qualitative nucleic acid fluorescence in situ hybridization (FISH) identification and quantitative, antimicrobial susceptibility testing (AST) methods and is intended for use with the Accelerate Pheno system. The Accelerate PhenoTest BC kit is capable of simultaneous detection and identification of multiple microbial targets followed by susceptibility testing of the appropriate detected bacterial organisms. The Accelerate PhenoTest BC

Device & Predicate Device(s):	VITEK REVEAL AST System and VITEK REVEAL GN AST Assay K230675	Accelerate Pheno System and PhenoTest BC Kit K192665
		kit is performed directly on blood culture samples identified as positive by a continuous monitoring blood culture system. Results are intended to be interpreted in conjunction with Gram stain results.
Indicated Organisms	Gram-negative organisms	Same
Type of Test	Automated incubation and reading	Same
Sample	Dilution (aliquot) from a positive blood culture as identified by a continuous monitoring blood culture system	Same
Inoculum Method	Manual	Same
General Device Characteristic Differences		
Time to AST Result	Approximately 8 hours	Approximately 7 hours
IVD Function	AST	ID and AST
AST Panel Preparation	Manual	Automated
Antimicrobial Agents	Amikacin Amoxicillin/clavulanate Ampicillin/sulbactam Aztreonam Cefepime Cefotaxime Cefotaxime/clavulanate Ceftazidime Ceftazidime/avibactam Ceftazidime/clavulanate Ceftolozane/tazobactam Ceftriaxone Cefuroxime Ciprofloxacin Ertapenem Gentamicin Imipenem	Amikacin Ampicillin/sulbactam Aztreonam Cefepime Ceftazidime Ceftriaxone Ciprofloxacin Ertapenem Gentamicin Meropenem Piperacillin/tazobactam Tobramycin

Device & Predicate Device(s):	VITEK REVEAL AST System and VITEK REVEAL GN AST Assay K230675	Accelerate Pheno System and PhenoTest BC Kit K192665
	Levofloxacin Meropenem Meropenem/vaborbactam Piperacillin/tazobactam Tetracycline Tobramycin Trimethoprim/ sulfamethoxazole	
Technology	Growth based analysis, using detection of metabolic byproducts	Morphokinetic cellular analysis (MCA)
Results	Report results as minimum inhibitory concentration (MIC), categorical interpretation, and ESBL determination	Report results as minimum inhibitory concentration (MIC), categorical interpretation

VI Standards/Guidance Documents Referenced:

1. CLSI Standard M07 11th Ed. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically (2018)
2. IEC 61326-1:2020 Electromagnetic Immunity, Conducted Immunity, and Class A Electromagnetic Radiation and Conducted Emissions
3. IEC 60601-1-2:2014+AMD1:2020 Electromagnetic Immunity, Medical Equipment
4. IEC 61326-2-6:2020 - Electrical equipment for measurement, control and laboratory use - EMC requirements – Part 2-6
5. IEC 61010-1: 2010 3rd Edition - Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1
6. IEC 61010-2-101:2018 3rd Edition - Safety requirements for electrical equipment for measurement, control, and laboratory use
7. IEC 61010-2-010:2019 4th Edition - Safety requirements for electrical equipment for measurement, control and laboratory use
8. FCC Part 15 Subpart B Electromagnetic Radiation and Conducted Emissions
9. CLSI supplement EP37. Supplemental Tables for Interference Testing in Clinical Chemistry 1st ed; 2018
10. CLSI supplement M100 32nd, 33rd, and 34th Ed. Performance Standards for Antimicrobial Susceptibility Testing; 2022, 2023, 2024
11. FDA Class II Special Controls Guidance Document: Antimicrobial Susceptibility (AST) Systems: Guidance for Industry and FDA (Issued August 28, 2009). General Principles of Software Validation; Final Guidance for Industry and FDA Staff

12. Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices. Issued May 11, 2005.
13. Electromagnetic Compatibility (EMC) of Medical Devices: Guidance for Industry and Food and Drug Administration Staff. Issued June 6, 2022.
14. Guidance for Industry: Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software. Issued January 14, 2005
15. Content of Premarket Submissions for Management of Cybersecurity in Medical Devices: Guidance for Industry and Food and Drug Administration Staff. Issued October 2, 2014
16. Post market Management of Cybersecurity in Medical Devices: Guidance for Industry and Food and Drug Administration Staff. Issued December 28, 2016.
17. Off-The-Shelf Software Use in Medical Devices: Guidance for Industry and Food and Drug Administration Staff. Issued September 27, 2019.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Reproducibility testing for the VITEK REVEAL GN AST Assay was conducted at three sites (two external and one internal site) by evaluating eighty-two (82) Gram-negative isolates, generally representing indicated organisms, that provided at least 10 organisms with on-scale MIC results for each antibiotic on the VITEK REVEAL Antibiotic panels. Isolates were tested in one of three VITEK REVEAL antibiotic panels (VITEK REVEAL SGN1, VITEK REVEAL SGN2, or VITEK REVEAL SGN3) as shown in **Table 1**. Each isolate was tested in triplicate over three days (≥10 isolates x 3 sites x 3 replicates x 3 days = ≥270 results per antibiotic). Isolates were spiked into blood culture bottles containing human blood and incubated until positivity. Three inoculum dilutions were prepared from each positive blood culture aliquot and used to inoculate the three VITEK REVEAL Antibiotic Panels. The mode of MIC values was determined for each isolate. Reproducibility was determined from the total number (and percent) of results that were within one dilution (+/- one doubling dilution) of the modal MIC result divided by the total number of results.

For trimethoprim/sulfamethoxazole, only five isolates were tested due to the lack of isolates with on-scale MICs; however, the five isolates were tested on six days rather than three to achieve the appropriate number of replicates.

Both best-case (assumes that off-scale results are less than one dilution from the mode) and worst-case (assumes that off-scale results are more than one dilution from the mode) performance was determined for each antimicrobial agent, as outlined in the AST Special Controls Guidance. The best-case reproducibility for each antimicrobial was ≥ 95%, which is acceptable. Worst-case reproducibility was ≥ 89% for all antibiotics, which is acceptable. Results of the reproducibility are summarized in **Table 2**.

Table 1. Plate configuration for the VITEK REVEAL AST System

VITEK REVEAL SGN1 Antibiotics	VITEK REVEAL SGN2 Antibiotics	VITEK REVEAL SGN3 Antibiotics
Ampicillin/sulbactam	Amikacin	Amoxicillin/clavulanate
Cefotaxime	Gentamicin	Cefepime
Ceftazidime	Tobramycin	Tetracycline
Ceftazidime/avibactam	Aztreonam	Ciprofloxacin
Ceftolozane/tazobactam	Ertapenem	Levofloxacin
Cefuroxime	Imipenem	
Ceftriaxone	Meropenem	
ESBL*	Meropenem/vaborbactam	
	Piperacillin/tazobactam	
	Trimethoprim/sulfamethoxazole	

*Assay used to determine extended-spectrum β-lactamase (ESBL) status for the species tested.

Table 2. Summary of results by antibiotic with best and worst-case reproducibility across all sites.

Antibiotic	**Best case #**	**Best case %**	**Worst case #**	**Worst case %**
Ampicillin/ sulbactam*	269/270	99.6%	266/270	98.5%
Cefotaxime	342/351	97.4%	342/351	97.4%
Ceftazidime*	395/396	99.7%	395/396	99.7%
Ceftazidime/ avibactam*	345/350	98.6%	345/350	98.6%
Ceftolozane/ tazobactam*	564/565	99.8%	564/565	99.8%
Cefuroxime	429/429	100.0%	427/429	99.5%
Ceftriaxone	267/267^	100.0%	259/267	97.0%
ESBL confirmation	529/540	98.0%	N/A	N/A
Amikacin	891/891	100.0%	870/891	97.6%
Gentamicin	538/538	100.0%	523/538	97.2%
Tobramycin	808/809	99.9%	807/809	99.8%
Aztreonam*	287/296	97.0%	287/296	97.0%
Ertapenem*	291/297	98.0%	291/297	98.0%
Imipenem	397/397	100.0%	364/397	91.7%
Meropenem	404/405	99.8%	395/405	97.5%
Meropenem/ vaborbactam	285/297	96.0%	285/297	96.0%
Piperacillin/ tazobactam	377/377	100.0%	368/377	97.6%
Trimethoprim/ sulfamethoxazole	269/269^	100.0%	263/269	97.8%

Antibiotic	Best case #	Best case %	Worst case #	Worst case %
Amoxicillin/ clavulanate	324/324	100.0%	323/324	99.7%
Cefepime	371/377	98.4%	360/377	95.5%
Tetracycline	297/297	100.0%	291/297	98.0%
Ciprofloxacin	319/324	98.5%	319/324	98.5%
Levofloxacin	323/323	100.0%	323/323	100.0%

*Analysis includes non-indicated species.
^ Indeterminate results generated from one or more isolates were excluded from the analysis.

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

Exogenous/Exogenous Interference Studies
An interfering substances study was performed to evaluate if substances naturally present or artificially introduced into blood culture bottles affect VITEK REVEAL GN AST Assay and VITEK REVEAL AST System performance. Organisms evaluated included representative strains of each indicated organism group: *Acinetobacter baumannii, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae*, and *Enterobacter cloacae*. Potential interferents were spiked into BD BACTEC Aerobic Plus blood culture bottles at or above clinically relevant concentrations along with representative organisms. Control bottles were seeded with organism and no potential interferent. Bottles were incubated in a continuous monitoring blood culture system until positivity. As this is a method-to-method comparison, determined by comparing MIC results from the interferent-containing samples with the modal MIC of the control samples, and essential agreement (EA) of ≥95% was deemed acceptable.

A total of 184 interferent-antibiotic combinations were tested on the VITEK REVEAL AST system. Overall, the presence of high concentrations of these interferents in blood cultures does not interfere with the results of the VITEK REVEAL AST system (**Tables 3 & 4**). There were a few instances in which EA was <95% for specific interferents, discussed below:

Ceftazidime in the presence of hemolysate (RBC), sodium citrate, and triglycerides (LPD) (tested individually) had an EA < 95% due to one replicate of *K. pneumoniae* being out of EA. In each instance, one replicate of *K. pneumoniae* was out of EA yet was within category agreement (CA), and thus is not expected to impact patient care. In addition, variable MIC values were attributed to this strain's growth pattern detection by the system. This is noted in a footnote in the device labeling.

Meropenem in the presence of heparin had an EA < 95% for *K. pneumoniae* due to one replicate being out of EA. However, this result is within category agreement (CA), and thus is not expected to impact patient care. This is noted in a footnote in the device labeling.

Meropenem/Vaborbactam in the presence of triglycerides (LPD) had an EA <95% for *E. cloacae* due to one replicate being out of EA. Upon repeat testing, the EA was found to be 100% This is noted in a footnote in the device labeling.

Meropenem/Vaborbactam in the presence of heparin had an EA <95% for *K. pneumoniae* due to one replicate being out of EA. However, this result is within category agreement (CA), and thus is not expected to impact patient care. This is noted in a footnote in the device labeling.

Ceftazidime/Avibactam in the presence of hemolysate (RBC) had an EA <95% for *P. aeruginosa* due to one replicate being out of EA. However, this result is within category agreement (CA), and thus is not expected to impact patient care. This is noted in a footnote in the device labeling.

Ceftriaxone in the presence of heparin had an EA <95% for *K. pneumoniae.* The low EA was due to one replicate being out of EA. Upon repeat testing, the EA was found to be 100%. This is noted in a footnote in the device labeling.

In addition, organisms with on-scale MIC values were not tested for several antibiotic/organism group combinations with all the potential interfering substances, except platelets. The following limitation is included in the device labeling:

Interference has not been established for the following drug/organism combination for all interferents, except platelets: amoxicillin-clavulanate/Enterobacterales, aztreonam/Enterobacterales, cefepime/Enterobacterales, ceftazidime/Enterobacterales, ceftriaxone/Enterobacterales, ciprofloxacin/*P. aeruginosa*, levofloxacin/*P. aeruginosa*, ertapenem/Enterobacterales, imipenem/Enterobacterales.

Table 3. Overall Performance with Potential Interferents (part 1).

Antimicrobial	Red Blood Cells (≥200 mg/mL)		White Blood Cells (≥ 1.2 x 10^7/mL)		Platelets (>400,000/µL)		Gamma Globulins (≥ 20 mg/mL)	
	# EA / Total	% EA	# EA / Total	% EA	# EA / Total	% EA	# EA / Total	% EA
Amikacin	15/15	100.0%	15/15	100.0%	48/48	100.0%	15/15	100.0%
Amoxicillin-Clavulanate	9/9	100.0%	9/9	100.0%	36/36	100.0%	9/9	100.0%
Ampicillin-Sulbactam	9/9	100.0%	9/9	100.0%	36/36	100.0%	9/9	100.0%
Aztreonam	12/12	100.0%	12/12	100.0%	45/45	100.0%	12/12	100.0%
Cefepime	12/12	100.0%	12/12	100.0%	42/42	100.0%	12/12	100.0%
Cefotaxime	12/12	100.0%	12/12	100.0%	42/42	100.0%	12/12	100.0%
Ceftazidime	14/15	93.3%*	15/15	100.0%	48/48	100.0%	15/15	100.0%
Ceftazidime/Avibactam	11/12	91.7%*	12/12	100.0%	45/45	100.0%	11/11	100.0%
Ceftolozane/Tazobactam	12/12	100.0%	12/12	100.0%	45/45	100.0%	12/12	100.0%
Ceftriaxone	9/9	100.0%	8/8	100.0%	39/39	100.0%	9/9	100.0%
Cefuroxime	6/6	100.0%	6/6	100.0%	33/33	100.0%	6/6	100.0%
Ciprofloxacin	12/12	100.0%	12/12	100.0%	42/42	100.0%	12/12	100.0%
Ertapenem	9/9	100.0%	8/8	100.0%	40/42	95.2%	9/9	100.0%
ESBL**	6/6	100.0%	6/6	100.0%	33/33	100.0%	6/6	100.0%
Gentamicin	12/12	100.0%	12/12	100.0%	45/45	100.0%	12/12	100.0%
Imipenem	15/15	100.0%	15/15	100.0%	48/48	100.0%	15/15	100.0%
Levofloxacin	12/12	100.0%	12/12	100.0%	42/42	100.0%	12/12	100.0%
Meropenem	15/15	100.0%	15/15	100.0%	48/48	100.0%	15/15	100.0%

Antimicrobial	Red Blood Cells (≥200 mg/mL)		White Blood Cells (≥ 1.2 x 10^7/mL)		Platelets (>400,000/µL)		Gamma Globulins (≥ 20 mg/mL)	
	# EA / Total	% EA	# EA / Total	% EA	# EA / Total	% EA	# EA / Total	% EA
Meropenem/Vaborbactam	9/9	100.0%	9/9	100.0%	42/42	100.0%	9/9	100.0%
Piperacillin/Tazobactam	15/15	100.0%	15/15	100.0%	48/48	100.0%	15/15	100.0%
Tetracycline	9/9	100.0%	9/9	100.0%	42/42	100.0%	9/9	100.0%
Tobramycin	12/12	100.0%	12/12	100.0%	45/45	100.0%	12/12	100.0%
Trimethoprim/Sulfamethoxazole	9/9	100.0%	9/9	100.0%	42/42	100.0%	9/9	100.0%

* Low EA was due to one replicate being out of EA yet was within category agreement (CA).
**Assay is qualitative. Values reported in the table are %CA.

Table 4. Overall Performance with Potential Interferents (part 2)

Antimicrobial	Conjugated bilirubin (≥ 0.02 mg/mL)		Triglycerides (≥ 15 mg/mL)		Heparin (≥ 3 units/mL)		Sodium Citrate (> 6% w/v)		Sodium Polyanetholesulfonate (> 2% w/v)	
	# EA / Total	% EA	# EA / Total	% EA	#EA/ Total	% EA	#EA/ Total	% EA	#EA/ Total	% EA
Amikacin	15/15	100.0%	15/15	100.0%	15/15	100.0%	15/15	100.0%	15/15	100.0%
Amoxicillin-Clavulanate	9/9	100.0%	9/9	100.0%	5/5	100.0%	5/5	100.0%	9/9	100.0%
Ampicillin-Sulbactam	9/9	100.0%	9/9	100.0%	9/9	100.0%	9/9	100.0%	9/9	100.0%
Aztreonam	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%
Cefepime	12/12	100.0%	12/12	100.0%	11/11	100.0%	11/11	100.0%	12/12	100.0%
Cefotaxime	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%
Ceftazidime	15/15	100.0%	13/15	86.7%*	15/15	100.0%	12/15	80.0%*	15/15	100.0%
Ceftazidime/Avibactam	11/11	100.0%	11/11	100.0%	11/11	100.0%	12/12	100.0%	12/12	100.0%
Ceftolozane/Tazobactam	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%
Ceftriaxone	9/9	100.0%	9/9	100.0%	8/9	88.9%^	9/9	100.0%	9/9	100.0%
Cefuroxime	6/6	100.0%	6/6	100.0%	6/6	100.0%	6/6	100.0%	6/6	100.0%
Ciprofloxacin	12/12	100.0%	12/12	100.0%	11/11	100.0%	11/11	100.0%	12/12	100.0%
Ertapenem	9/9	100.0%	8/8	100.0%	9/9	100.0%	9/9	100.0%	9/9	100.0%
ESBL**	6/6	100.0%	6/6	100.0%	6/6	100.0%	6/6	100.0%	6/6	100.0%
Gentamicin	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%
Imipenem	15/15	100.0%	15/15	100.0%	15/15	100.0%	15/15	100.0%	15/15	100.0%
Levofloxacin	12/12	100.0%	12/12	100.0%	12/12	100.0%	11/11	100.0%	10/10	100.0%
Meropenem	15/15	100.0%	15/15	100.0%	14/15	93.3%*	15/15	100.0%	15/15	100.0%
Meropenem/Vaborbactam	15/15	100.0%	8/9	88.9%^	8/9	88.9%*	9/9	100.0%	9/9	100.0%
Piperacillin/Tazobactam	15/15	100.0%	15/15	100.0%	15/15	100.0%	15/15	100.0%	15/15	100.0%
Tetracycline	9/9	100.0%	9/9	100.0%	8/8	100.0%	8/8	100.0%	9/9	100.0%
Tobramycin	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%	12/12	100.0%
Trimethoprim/Sulfamethoxazole	9/9	100.0%	9/9	100.0%	9/9	100.0%	9/9	100.0%	9/9	100.0%

* Low EA was due to one replicate being out of EA yet was within category agreement (CA).
** Assay is qualitative. Values reported in the table is %CA.
^ Upon repeat testing, %EA was 100%.

Antimicrobial Interference Studies:
VITEK REVEAL GN AST Assay and VITEK REVEAL AST System performance was assessed using seeded positive blood culture samples with and without interfering antimicrobials. At least one representative organism from each claimed organism reporting group (i.e., *Proteus mirabilis*, *Escherichia coli*, *Acinetobacter baumannii*, *Enterobacter cloacae*, *Citrobacter freundii*, and *Serratia marcescens*) were evaluated with each claimed antimicrobial. One (1) antibiotic from nine (9) of the main classes of antibiotics that target Gram-negative organisms was tested as the interfering agent (i.e., ampicillin, ampicillin/sulbactam, aztreonam, cefotaxime, meropenem, ciprofloxacin, trimethoprim/sulfamethoxazole, tetracycline, and gentamicin). Antimicrobial interferents were spiked into blood culture bottles at or above clinically relevant concentrations along

with relevant organisms. A minimum of one (1) Gram-negative strain resistant to each interfering antimicrobial was tested in triplicate in BD BACTEC Standard aerobic bottles, which do not contain resins and do not have neutralization capabilities. Control bottles were seeded with organism and no antimicrobial interferent. Bottles were incubated in a continuous monitoring blood culture system until positivity. As this is a method-to-method comparison, essential agreement (EA) of ≥95% was deemed acceptable.

A total of 229 antimicrobial interferent-antibiotic combinations were tested on the VITEK REVEAL AST System. In general, the data were acceptable with 100% EA. There was one instance in which EA was <95% for a specific interferent, discussed below:

When the interferent ampicillin/sulbactam (150/88 µg/ml) was incubated with *E. coli*, ertapenem (EA 50%), meropenem (EA 66.7%), piperacillin/tazobactam (EA 66.7%), and trimethoprim/sulfamethoxazole (EA 83.3%) demonstrated an EA less than 95%. Based on growth patterns for these instances, it appears the ampicillin/sulbactam was interfering with the growth of the *E. coli*. Testing was repeated with a lower concentration of ampicillin/sulbactam (75/44 µg/ml) and the interference was not observed. In addition, a second *E. coli* strain was tested and the interference was not observed. This suggests that interference from ampicillin/sulbactam is possible for some *E. coli* strains and may be strain specific. This is noted in a footnote in the device labeling.

The following antibiotic pairs were not evaluated due to intrinsic resistance of the strains tested or the test was not indicted: ampicillin with tetracycline, imipenem, and trimethoprim/sulfamethoxazole; cefotaxime with ESBL; meropenem with ESBL; gentamicin with amoxicillin/clavulanate, ampicillin/sulbactam, cefuroxime, ESBL, piperacillin/tazobactam, imipenem, and ceftolozane/tazobactam; tetracycline with amoxicillin/clavulanate, ampicillin/sulbactam, ceftolozane/tazobactam, cefuroxime, and ESBL; trimethoprim/sulfamethoxazole and ESBL; and ciprofloxacin with ESBL.

4. Assay Reportable Range:

   Not applicable

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

   Quality Control Testing. Quality control testing was performed each day that testing was conducted. CLSI recommended or independently validated QC strains for each antimicrobial were tested a sufficient number of times (i.e., at least 20 times/site) at each testing site using the VITEK REVEAL AST System and at the reference site using the broth microdilution reference method.

   For all antimicrobials, greater than 95% of results were within the expected range, which is acceptable (**Table 5.**).

Table 5. QC Expected Ranges and Results for the VITEK REVEAL GN AST Assay

Antimicrobial	QC Organism	VITEK REVEAL Expected Range (µg/mL)	No. in Range (%)	
			Reference	VITEK REVEAL AST
Amikacin	*E. coli* ATCC 25922	≤ 0.5-4	104/104 (100%)	179/183 (97.8%)
	P. aeruginosa ATCC 27853	1-4	105/105 (100%)	176/176 (100%)
Amoxicillin-Clavulanate	*E. coli* ATCC 25922*	≤2/1-8/4	95/95 (100%)	175/178 (98.3%)
	K. pneumoniae ATCC 700603	4/4-16/8	92/92 (100%)	166/166 (100%)
Ampicillin-Sulbactam	*E. coli* ATCC 25922*	≤2/1-8/4	98/98 (100%)	183/186 (98.4%)
	K. pneumoniae ATCC 700603	8/4-32/16	92/92 (100%)	165/165 (100%)
Aztreonam	*E. coli* ATCC 25922*	≤0.25	103/104 (99.0%)	176/179 (98.3%)
	P. aeruginosa ATCC 27853	2-8	101/105 (96.2%)	177/177 (100%)
	K. pneumoniae ATCC 700603	8-64	99/101 (98.0%)	163/164 (99.3%)
Cefepime	*E. coli* ATCC 25922*	≤0.125	110/113 (97.3%)	174/177 (98.3%)
	P. aeruginosa ATCC 27853	0.5-4	113/113 (100%)	181/181 (100%)
	K. pneumoniae ATCC 700603	0.5-2	108/109 (99.1%)	165/165 (100%)
Cefotaxime	*E. coli* ATCC 25922*	≤0.25	113/116 (97.4%)	183/186 (98.4%)
	P. aeruginosa ATCC 27853	8-32	108/114 (94.7%)	171/174 (98.3%)
Ceftazidime	*E. coli* ATCC 25922*	≤0.125-0.5	114/116 (98.3%)	184/187 (98.4%)
	P. aeruginosa ATCC 27853	1-4	112/114 (98.2%)	170/171 (99.4%)
	K. pneumoniae ATCC 700603	16-64	109/109 (100%)	163/164 (99.4%)
Ceftazidime-Avibactam	*E. coli* ATCC 25922*	≤0.06/4-0.5/4	115/116 (99.1%)	184/187 (98.4%)
	P. aeruginosa ATCC 27853	0.5/4-4/4	113/114 (99.1%)	175/175 (100%)
	K. pneumoniae ATCC 700603	0.25/4-2/4	107/109 (98.2%)	164/165 (99.4%)

Antimicrobial	QC Organism	VITEK REVEAL Expected Range (µg/mL)	No. in Range (%)	
			Reference	VITEK REVEAL AST
Ceftolozane-Tazobactam	*E. coli* ATCC 25922	0.125/4-0.5/4	125/128 (97.7%)	183/186 (98.4%)
	P. aeruginosa ATCC 27853	0.25/4-1/4	121/126 (96.0%)	175/175 (100%)
	K. pneumoniae ATCC 700603	0.5/4-2/4	117/120 (97.5%)	164/164 (100%)
Ceftriaxone	*P. aeruginosa* ATCC 27853*	8->16	114/114 (100%)	174/174 (100%)
	K. pneumoniae ATCC 700603**	2-8	103/107 (96.3%)	163/163 (100%)
Cefuroxime	*E. coli* ATCC 25922	2-8	106/106 (100%)	182/186 (97.8%)
Ciprofloxacin	*E. coli* ATCC 25922*	≤0.0625	110/113 (97.3%)	175/178 (98.3%)
	P. aeruginosa ATCC 27853	0.125-1	111/113 (98.2%)	177/182 (97.3%)
Ertapenem	*E. coli* ATCC 25922*	≤0.125	111/113 (98.2%)	178/182 (97.8%)
	P. aeruginosa ATCC 27853	2-8	108/114 (94.7%)	175/176 (99.4%)
Gentamicin	*E. coli* ATCC 25922*	≤0.25-1	103/104 (99.0%)	183/183 (100%)
	P. aeruginosa ATCC 27853	0.5-2	104/105 (99.0%)	177/177 (100%)
Imipenem	*E. coli* ATCC 25922*	≤0.25-0.5	103/104 (99.0%)	178/182 (97.8%)
	P. aeruginosa ATCC 27853	1-4	104/105 (99.0%)	174/175 (99.4%)
	K. pneumoniae ATCC 700603*	≤0.25-0.5	100/101 (99.0%)	164/164 (100%)
Levofloxacin	*E. coli* ATCC 25922*	≤0.125	111/113 (98.2%)	176/178 (98.8%)
	P. aeruginosa ATCC 27853	0.5-4	111/113 (98.2%)	174/182 (95.6%)
Meropenem	*E. coli* ATCC 25922*	≤0.0625	104/104 (100%)	179/183 (97.8%)
	P. aeruginosa ATCC 27853	0.125-1	104/105 (99.0%)	175/176 (99.4%)
	K. pneumoniae ATCC BAA-2814*	≥32	98/98 (100%)	196/197 (99.4%)
Meropenem-Vaborbactam	*E. coli* ATCC 25922*	≤0.0625/8	103/104 (99.0%)	179/183 (97.8%)

Antimicrobial	QC Organism	VITEK REVEAL Expected Range (µg/mL)	No. in Range (%)	
			Reference	VITEK REVEAL AST
	P. aeruginosa ATCC 27853	0.125/8-1/8	103/105 (98.1%)	177/178 (99.4%)
	K. pneumoniae ATCC 700603*	≤0.0625/8	100/101 (99.0%)	165/165 (100%)
	K. pneumoniae ATCC BAA-2814	0.125/8-0.5/8	89/98^ (90.8%)	190/197 (96.4%)
Piperacillin-Tazobactam	*E. coli* ATCC 25922*	≤2/4-8/4	111/112 (99.1%)	178/183 (95.7%)
	P. aeruginosa ATCC 27853*	≤2/4-8/4	112/114 (98.2%)	177/177 (100%)
	K. pneumoniae ATCC 700603	8/4-32/4	107/109 (98.2%)	165/165 (100%)
Tetracycline	*E. coli* ATCC 25922*	≤1-2	95/95 (100%)	178/178 (100%)
	P. aeruginosa ATCC 27853	8-32	95/95 (100%)	173/181 (95.5%)
Tobramycin	*E. coli* ATCC 25922	0.25-1	102/104 (98.1%)	179/184 (97.3%)
	P. aeruginosa ATCC 27853	0.25-1	105/105 (100%)	177/177 (100%)
Trimethloprim-Sulfamethoxazole	*E. coli* ATCC 25922	≤0.5/9.5	102/104 (98.1%)	182/182 (100%)
	P. aeruginosa ATCC 27853	8/52-32/608	102/105 (97.1%)	174/177 (98.3%)

*VITEK REVEAL expected results are partially or entirely off-scale. Off-scale results were considered acceptable.
** Validation performed for non-CLSI recommended QC strain.
^ Clinical data on days with out-of-range QC results was considered acceptable due to alternative QC strains that tested in-range on the same day.

QC expected and actual results for ESBL determination are summarized in **Table 6.** The VITEK REVEAL AST System demonstrated 100% concordance with expected results. Overall, QC was determined to be acceptable.

Table 6. QC Results for the VITEK REVEAL AST System for ESBL Determination

Antimicrobial	**QC Organism**	**Expected Result**	**No. Correct (%)**	
			Reference	**REVEAL**
ESBL Screen	*E. coli* ATCC 25922	Negative	94/94 (100)	183/183 (100)
ESBL Screen	*K. pneumoniae* ATCC 700603	Positive	88/88 (100)	157/157 (100)

Validation of *K. pneumoniae* ATCC 700603 as an Additional QC Organism for Ceftriaxone on the VITEK REVEAL

To validate the use of *K. pneumoniae* ATCC 700603 as a QC organism with the VITEK REVEAL, 24 replicates of *K. pneumoniae* ATCC 700603 were tested per two lots of the

antimicrobial reagents over two days resulting in 96 data points to determine the BMD range for this combination. All data points fell between 2-8 µg/ml. In the clinical study, an additional 107 data points were tested by BMD for a total of 203 data points with >95% in-range, which supported a QC range of 2-8 µg/ml in the VITEK REVEAL clinical study. When *K. pneumoniae* ATCC 700603 was tested on the VITEK REVEAL, 217/217 (100%) of the results fell within the QC range of 2-8 µg/ml. Taken together, these data are acceptable to support the use of *K. pneumoniae* ATCC 700603 as a QC organism when testing ceftriaxone on the VITEK REVEAL.

Purity Check
Purity plates were prepared from the positive blood cultures of every sample tested. AST results were only reported for pure isolates; data generated from plates that generated multiple colony morphologies was excluded from analyses.

Device Failure
Seven device failures were observed during validation studies. All were detected at the time of failure by the system and resulted in error messages, thus had no impact on results. Two failures were due to undefined internal system failures resulting in no result reports generated. Three failures were due to no MIC calls due to the system timing out without a result reported. Two failures were technical errors due to a suspected sample switch.

Growth Failure Rate
There were four growth failures (failed on all three antibiotic panels) on the VITEK REVEAL AST System and one partial growth failure (failed on only one of the three antibiotic panels).

Specimen Stability
The purpose of this study was to demonstrate that positive blood cultures tested up to 16 hours post positivity (T16) and held at room temperature (RT) or in the blood culture instrument (36°C-37°C) provide accurate results.

Contrived positive blood culture specimens (prepared in BD BACTEC Plus Aerobic/F blood culture bottles and BACT/ALERT FA PLUS Aerobic bottles) containing the recommended blood volume were tested at T0, T8 (eight-ten hours post-positivity), and T16 (16-18 hours post-positivity). Testing up to 18 hours was performed to support the stability at 16 hours post-positivity. Testing was performed in triplicate for each sample at each timepoint and each temperature condition. Resulting MICs were compared to the historical modal broth microdilution MIC. The acceptance criterion was ≥ 89% agreement for EA when compared to the modal MIC of the broth microdilution method. When the EA was below 89%, the modal MIC for the incubation condition and time points was compared to the T0 MIC result to assess the discrepancy. QC was performed each day of testing.

A total of 25 gram-negative isolates with known MICs as determined by broth microdilution testing were evaluated. Species tested included *Acinetobacter baumannii* (1), *E. coli* (6), *K. pneumoniae* (2), *K. aerogenes* (5), *K. oxytoca* (3), *P. mirabilis* (2), *S. marcescens* (1) and *P. aeruginosa* (5). Results for all antimicrobials tested were acceptable for stability up to 16 hours when applying the acceptance criteria (**Tables 7 & 8**) except for the instances below:

- Cefuroxime and *E. coli* at T8 (36°C-37°C) in the BD BACTEC Plus Aerobic/F blood culture bottles,
- Cefuroxime and *E. coli* at T0 (36°C-37°C and RT), T8 (RT) and T16 (RT) in the BACT/ALERT FA PLUS Aerobic bottles, and
- ESBL analysis (CA) and *E. coli* for all conditions except T8 (RT) in the BD BACTEC Plus Aerobic/F bottles.

All instances resulted in an EA/CA of 100% based on comparisons between the T0 and other timepoints obtained by the VITEK REVEAL system. This is noted in a footnote in the device labeling.

As noted in the instructions for use, all blood culture bottle samples should be tested promptly after ringing positive on a continuous monitoring system. In the case of unavoidable delays or if the need for re-testing arises, positive blood culture bottles may be tested up to 16 hours post ring.

Table 7. Summary of Sample Stability AST Results at T0, T8, and T16 as compared to the BMD Mode for BD BACTEC Plus Aerobic/F.

Antimicrobial	Instrument (36°C-37°C) No. EA/Total Tested (EA%)			Bench (RT) No. EA/Total Tested (EA%)		
	T0	T8	T16	T0	T8	T16
Ampicillin/Sulbactam	18/18 (100%)	16/16 (100%)	18/18 (100%)	18/18 (100%)	18/18 (100%)	18/18 (100%)
Cefotaxime	27/27 (100%)	25/25 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
Ceftazidime	28/29 (96.5%)	29/29 (100%)	30/30 (100%)	28/29 (96.5%)	30/30 (100%)	30/30 (100%)
Ceftazidime/Avibactam	27/27 (100%)	26/26 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
Ceftolozane/Tazobactam	27/27 (100%)	26/26 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
Ceftriaxone	22/24 (91.7%)	24/24 (100%)	24/24 (100%)	22/24 (91.7%)	24/24 (100%)	24/24 (100%)
Cefuroxime	15/15 (100%)	12/14* (85.7%)	14/15 (93.3%)	15/15 (100%)	15/15 (100%)	15/15 (100%)
ESBL**	11/14* (78.6%)	12/14* (85.7 %)	13/15* (86.6%)	11/14* (78.6%)	15/15 (100%)	12/15* (80.0%)
Amikacin	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
Aztreonam	29/30 (96.7%)	29/30 (96.7%)	30/30 (100%)	29/30 (96.7%)	27/29 (93.1%)	30/30 (100%)
Ertapenem	24/24 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)	24/24 (100%)	23/23 (100%)
Gentamicin	30/30 (100%)	28/30 (93.3%)	30/30 (100%)	30/30 (100%)	28/30 (93.3%)	29/30 (96.7%)
Imipenem	27/27 (100%)	26/26 (100%)	26/26 (100%)	27/27 (100%)	25/26 (96.1%)	26/26 (100%)

Antimicrobial	Instrument (36°C-37°C) No. EA/Total Tested (EA%)			Bench (RT) No. EA/Total Tested (EA%)		
	T0	T8	T16	T0	T8	T16
Meropenem	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	29/30 (96.7%)	29/29 (100%)
Meropenem/Vaborbactam	24/24 (100%)	23/24 (95.8%)	24/24 (100%)	24/24 (100%)	22/23 (95.6%)	23/23 (100%)
Piperacillin/Tazobactam	28/30 (93.3%)	30/30 (100%)	30/30 (100%)	28/30 (93.3%)	29/30 (96.7%)	30/30 (100%)
Tobramycin	30/30 (100%)	27/30 (90.0%)	30/30 (100%)	30/30 (100%)	29/30 (96.7%)	30/30 (100%)
Trimethoprim/ Sulfamethoxazole	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)
Amoxicillin/Clavulanate	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	11/11 (100%)	12/12 (100%)
Cefepime	24/24 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)
Ciprofloxacin	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)
Levofloxacin	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)
Tetracycline	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)

* As described above, comparison to T0 and other timepoints resulted in an EA/CA of 100%.
** Assay is qualitative. Values reported in the table is %CA.

Table 8. Summary of Sample Stability AST Results at T0, T8, and T16 as compared to the BMD Mode for BACT/ALERT FA PLUS Aerobic.

Antimicrobial	Instrument (36°C-37°C) No. EA/Total Tested (EA%)			Bench (RT) No. EA/Total Tested (EA%)		
	T0	T8	T16	T0	T8	T16
Ampicillin/Sulbactam	18/18 (100%)	18/18 (100%)	18/18 (100%)	18/18 (100%)	18/18 (100%)	18/18 (100%)
Cefotaxime	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
Ceftazidime	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
Ceftazidime/Avibactam	27/27 (100%)	27/27 (100%)	26/27 (96.3%)	27/27 (100%)	26/27 (96.3%)	27/27 (100%)
Ceftolozane/Tazobactam	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	26/27 (96.3%)	26/26 (100%)
Ceftriaxone	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)
Cefuroxime	12/15* (80.0%)	15/15 (100%)	14/15 (93.3%)	12/15* (80.0%)	13/15 (86.7%)	12/15 (80.0%)
ESBL**	15/15 (100%)	15/15 (100%)	14/15 (93.3%)	15/15 (100%)	15/15 (100%)	15/15 (100%)

Antimicrobial	Instrument (36°C-37°C) No. EA/Total Tested (EA%)			Bench (RT) No. EA/Total Tested (EA%)		
	T0	T8	T16	T0	T8	T16
Amikacin	30/30 (100%)	30/30 (100%)	27/30 (90.0%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
Aztreonam	27/30 (90.0%)	30/30 (100%)	30/30 (100%)	27/30 (90.0%)	30/30 (100%)	29/29 (100%)
Ertapenem	24/24 (100%)	24/24 (100%)	23/23 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)
Gentamicin	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
Imipenem	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)	27/27 (100%)
Meropenem	30/30 (100%)	29/30 (96.7%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
Meropenem/Vaborbactam	22/24 (91.7%)	24/24 (100%)	24/24 (100%)	22/24 (91.7%)	24/24 (100%)	24/24 (100%)
Piperacillin/Tazobactam	30/30 (100%)	29/30 (96.7%)	27/30 (90.0%)	30/30 (100%)	30/30 (100%)	27/30 (90.0%)
Tobramycin	29/29 (100%)	28/30 (93.3%)	30/30 (100%)	30/30 (100%)	30/30 (100%)	30/30 (100%)
Trimethoprim/ Sulfamethoxazole	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)
Amoxicillin/Clavulanate	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)
Cefepime	24/24 (100%)	23/23 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	23/23 (100%)
Ciprofloxacin	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)
Levofloxacin	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)	24/24 (100%)
Tetracycline	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)

* As described above, comparison to T0 and other timepoints resulted in an EA/CA of 100%.
** Assay is qualitative. Values reported in the table is %CA.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Not applicable

8. Accuracy (Instrument):

   Not applicable

9. Carry-Over:

Crosstalk Study:
The purpose of this study was to assess whether volatile organic compounds (VOC's) emitted by growing bacteria are exchanged between adjacent wells on the same panel during testing with the VITEK REVEAL GN Assay and the VITEK REVEAL AST System. Contrived positive blood cultures containing one of five organisms (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *P. mirabilis*, and *A. baumannii*) were tested in a checkerboard pattern with media-only. The five organisms were rotated over 20 days to generate 4 replicate plates for each bacterial organism using a different analyzer and sealer each day of testing. VOC's were detected in the media-only wells one time (1) out of 960 wells tested for a contamination rate of 0.1%, which is acceptable.

Carryover Study:
The purpose of this study was to evaluate the potential for organism or VOC carryover between VITEK REVEAL GN Assay panels run on the same VITEK REVEAL AST System. Following the processing of a contrived positive blood culture panel, a media-only panel was processed on the same instrument and sealer. Twenty (20) media only panels were processed and VOC's were detected in one (1) out of 1920 wells tested. This is a contamination rate of less than 0.1%, which is acceptable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Clinical performance testing on the VITEK REVEAL AST System using the VITEK REVEAL GN Assay was performed at five external, geographically diverse, U.S. clinical test sites. The broth microdilution testing was performed at a single reference site. Challenge isolate testing was performed at two internal sites. Performance was evaluated using fresh (prospective) positive blood cultures, as well as positive blood culture samples contrived with clinical stock isolates and challenge isolates. The challenge isolates were selected for their resistance profiles. Positive blood cultures confirmed by Gram stain to contain only Gram-negative rods were enrolled into the study.

Organism identification was obtained from an FDA cleared molecular bacterial identification method and/or FDA cleared MALDI TOF method for input into the VITEK REVEAL AST System. The species identification provided by the clinical site was confirmed at the reference site using an FDA-cleared MALDI identification method. Any samples with a species identification at the reference site not matching the expected ID or found to be polymicrobial did not proceed to BMD testing.

A total of 1,115 positive blood cultures (424 fresh (prospective), 101 seeded with stock organisms, and 590 seeded with challenge organisms) were tested to evaluate the VITEK REVEAL AST System performance for 22 antimicrobials and one screening test, ESBL, using the VITEK REVEAL GN Assay. Depending on the spectrum of activity, breakpoints, and the claimed organisms (species/group) for each antimicrobial on the panel, the number of datapoints for the various antimicrobial-organisms tested varied. VITEK REVEAL results were compared to the modal value of triplicate broth microdilution reference results performed at an independent reference laboratory.

Performance was determined generally based on criteria outlined in the Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems including essential agreement (EA), categorical agreement (CA), and categorical errors (minor, major and very major errors). EA was calculated as the percentage of VITEK REVEAL MIC results that were within plus or minus one serial two-fold dilution of the reference result. CA was calculated as the percentage of VITEK REVEAL interpretive results (S/I/R) that were identical to the interpretive results of the reference result. EA of evaluable results (on-scale VITEK REVEAL and reference results or results in which an off-scale result was at least two doubling dilutions from the on-scale result) were also calculated. Performance was considered acceptable if the EA and CA were ≥90%, major error rate was ≤3%, and very major error rate was ≤2%. For antimicrobials that lack an intermediate interpretive result, further analysis of the category errors was performed, and adjustments were made by considering the MIC values that were one doubling dilution from the reference MIC value.

A high-level summary of the performance of the VITEK REVEAL AST System is described below for each antimicrobial and indicated species. Complete details and results including EA, CA and error rate analyses are summarized below in **Tables 9** and **10.**

Amikacin. A total of 756 specimens (299 *E. coli,* 123 *K. pneumoniae* group*,* 40 *K. oxytoca,* 48 *K. aerogenes,* 39 *E. cloacae* complex*,* 23 *C. freundii complex,* 31 *P. mirabilis,* 28 *S. marcescens*, 60 *A. baumannii-calcoaceticus* complex, and 65 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 98.1% and CA of 99.4%. There were four (4) minor (0.6%), no major and no very major errors. Overall, performance is acceptable.

The *A. baumannii-calcoaceticus* results from clinical and challenge testing demonstrated an EA of 90% and CA of 88.3%. There were seven (7) minor (11.7%), no major and no very major errors. The low CA was due to seven (7) minor errors with six (6) of the minor errors being in essential agreement. The following statement is included as a limitation in the device labeling to address the minor errors:

> For amikacin, perform an alternative method of testing prior to reporting of results for *A. baumannii-calcoaceticus* complex when the MIC is 32 µg/mL due to the occurrence of minor errors, that were in essential agreement, resulting in a category agreement below 90%.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 95.4% and CA of 95.4%. There were three (3) minor (4.6%), no major and no very major errors. Overall, performance is acceptable.

Amoxicillin/Clavulanate. A total of 500 Enterobacterales specimens (302 *E. coli*, 124 *K. pneumoniae* group, 41 *K. oxytoca*, and 33 *P. mirabilis*) were evaluated. The results from clinical and challenge testing demonstrated an EA of 95% and CA of 90.8%. There were 43 minor (8.6%), 3 major (0.7%) and no very major errors. Overall, performance is acceptable.

When evaluating results by individual species, thirty-five (35) of the minor errors were due to *E. coli*. The EA was 94.4% and the CA was 88%. There were 35 minor (11.6%), one (1) major (0.4%) and no very major errors. The low CA was due to the 35 minor errors with 29

of the minor errors being in essential agreement. The following statement is included as a limitation in the device labeling to address the minor errors:

> For amoxicillin/clavulanate, perform an alternative method of testing prior to reporting of results for *E. coli* when the MIC is 16 µg/mL due to the occurrence of minor errors, that were in essential agreement, resulting in a category agreement below 90%.

Ampicillin/Sulbactam. A total of 372 Enterobacterales specimens (300 *E. coli*, 40 *K. oxytoca*, and 32 *P. mirabilis*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 97.8% and CA of 77.2%. According to the AST Special Controls document, a CA <90.0% caused by a high number of minor errors is acceptable when very good EA of evaluable results are observed. The EA of evaluable results was high at 95.6%. There were 82 minor (22.0%), three (3) major (1.2%) and no very major errors. Overall, performance is acceptable.

To address the low CA, the following statement is included as a footnote to the AST performance table:

> The majority of ampicillin/sulbactam CA errors for Enterobacterales were minor errors.

When evaluating results by individual species, sixty-six (66) of the minor errors (22.0%) were due to *E. coli*, which demonstrated an EA of 97.3% and the CA of 77.1%. There were three (3) major (1.5%) and no very major errors. The EA of evaluable results was 94.3%. In addition, fourteen (14) of the minor errors (35.0%) were due to *K. oxytoca*. There were no major and no very major errors. The EA is 100% and the CA is 65% with an EA of evaluable isolates at 100%. There were no major and no very major errors. According to the AST Special Controls document, a CA <90.0% caused by a high number of minor errors is acceptable when very good EA of evaluable results are observed; therefore, performance for *E. coli* and *K. oxytoca* is acceptable.

Aztreonam. A total of 595 specimens (295 *E. coli,* 127 *K. pneumoniae* group*,* 43 *K. oxytoca,* 39 *E. cloacae* complex*,* 26 *C. freundii* complex and 65 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 97.4% and CA of 96.0%. There were 18 minor (3.4%), 3 major (0.8%) and no very major errors. Overall, performance is acceptable.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 96.9% and CA of 86.2%. According to the AST Special Controls document, a CA <90.0% caused by a high number of minor errors is acceptable when very good EA of evaluable results are observed. The EA of evaluable results was high at 96.1%, which is acceptable. There were nine (9) minor (13.8%), no major and no very major errors. Overall, performance is acceptable.

To address the low CA, the following statement is included as a footnote to the AST performance table:

> All aztreonam CA errors for *P. aeruginosa* were minor errors.

Cefepime. A total of 645 specimens (301 *E. coli,* 121 *K. pneumoniae* group*,* 40 *K. oxytoca,* 46 *K. aerogenes,* 35 *E. cloacae* complex*,* 36 *C. koseri* and 66 *P. aeruginosa*) were evaluated.

The Enterobacterales results from clinical and challenge testing demonstrated an EA of 96.0% and CA of 95.9%. There were 21 minor (3.6%), 3 major (0.7%) and no very major errors. Overall, performance is acceptable.

When evaluating results by individual species, *E. cloacae* complex results from clinical and challenge testing demonstrated an EA of 97.2% and CA of 88.9%. There were four (4) minor (11.4%), no major and no very major errors. According to the AST Special Controls document, a CA <90.0% caused by a high number of minor errors is acceptable when very good EA of evaluable results are observed. The EA of evaluable results was high at 94.4%, which is acceptable.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 97.0% and CA of 97.0%. There were two (2) major (6.1%) errors and no very major errors. The two major errors had an MIC value that was in essential agreement with the reference MIC. Therefore, due to the lack of an intermediate interpretive criterion, the adjusted major error rate was 0%, which is acceptable. Overall, performance is acceptable.

Cefotaxime. A total of 592 specimens (303 *E. coli,*123 *K. pneumoniae* group*,* 42 *K. oxytoca,* 47 *K. aerogenes,* 39 *E. cloacae* complex*,* and 38 *A. baumannii-calcoaceticus*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 97.3% and CA of 99.1%. There were three (3) minor (0.5%), two (2) major (0.5%) and no very major errors. Overall, performance is acceptable.

The *A. baumannii-calcoaceticus* results from clinical and challenge testing demonstrated an EA of 100% and CA of 100%. There were no minor, no major errors, and no very major errors. Overall, performance is acceptable. The following statement is included as a footnote to the AST performance table to address the lack of testing susceptible isolates:

> No cefotaxime susceptible strains were evaluated for *A. baumannii-calcoaceticus* complex. Cefotaxime susceptibility is rare in *A. baumannii-calcoaceticus* complex.

Ceftazidime. A total of 619 specimens (302 *E. coli,* 123 *K. pneumoniae group,* 40 *K. oxytoca,* 47 *K. aerogenes,* 38 *E. cloacae* complex*,* 30 *C. koseri* and 39 *A. baumannii-calcoaceticus*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 95.3% and CA of 97.1%. There were 16 minor (2.8%), one (1) major (0.2%) and no very major errors. Overall, performance is acceptable.

The *A. baumannii-calcoaceticus* results from clinical and challenge testing demonstrated an EA of 97.4% and CA of 94.9%. There were two (2) minor (5.1%), no major errors and no very major errors. Overall, performance is acceptable.

Ceftazidime/Avibactam. A total of 717 clinical specimens (301 *E. coli,* 124 *K. pneumoniae group,* 67 *K. aerogenes,* 39 *E. cloacae* complex*,* 24 *C. freundii* complex*,* 30 *C. koseri,* 39 *P. mirabilis* and 93 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 95.7% and CA of 99.7%. There were one (1) major (0.2%) error and one (1) very major (1.9%) error. Overall, performance is acceptable.

When evaluating results by individual species, *K. aerogenes* demonstrated an EA of 91.0% and CA of 98.5%. There were no major errors and one (1) very major (33.3%) error. The one

(1) very major error had an MIC value that was in essential agreement with the reference MIC. Therefore, due to the lack of an intermediate interpretive criterion, the adjusted very major error rate was 0%, which is acceptable. Overall, performance is acceptable.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 97.8% and CA of 97.8%. There were no minor, two (2) major (3%) errors and no very major errors. Overall, performance is acceptable.

Ceftolozane/Tazobactam. A total of 576 specimens (293 *E. coli,* 40 *K. oxytoca,* 45 *K. aerogenes,* 37 *E. cloacae complex,* 42 *C. koseri,* 31 *P. mirabilis,* 22 *P. vulgaris* and 66 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 92.9% and CA of 97.6%, which is acceptable. There were 10 minor errors (2.0%), one (1) major (0.2%) error and one (1) very major (1.5%) error. Overall, performance is acceptable.

When evaluating results by individual species, for *K. aerogenes* the EA was 93.3% and CA was 88.9%. There were five (5) minor (11.0%), no major and no very major errors. According to the AST Special Controls document, a CA <90.0% caused by a high number of minor errors is acceptable when very good EA of evaluable results are observed. The EA of evaluable results was 92.3%, which is acceptable.

For *K. oxytoca*, the EA was 95% and the CA was 97.5%. There were no minor, no major and one (1) very major (33%) error. The one (1) very major error was considered a random error due to the limited number of resistant isolates tested. This performance is acceptable.

For *P. aeruginosa* the results from clinical and challenge testing demonstrated an EA of 100% and CA of 98.5%. There were one (1) minor (1.5%), no major and no very major errors. Overall, performance is acceptable.

Ceftriaxone. A total of 626 specimens (294 *E. coli*, 132 *K. pneumoniae* group, 47 *K. oxytoca*, 52 *K. aerogenes*, 46 *E. cloacae* complex, and 55 *P. mirabilis*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 97.1% and CA of 96.6%. There were 18 minor (2.9%), three (3) major (0.7%) and no very major errors. Overall, performance is acceptable.

Cefuroxime. A total of 522 specimens (300 *E. coli*, 119 *K. pneumoniae* group, 40 *K. oxytoca*, 27 *C. koseri*, and 36 *P. mirabilis*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 95.8% and CA of 97.3%. There were no minor, 13 major (3.5%) errors and one (1) very major (0.7%) error. Four (4) major errors had an MIC value that was in essential agreement with the reference MIC. Therefore, due to the lack of an intermediate interpretive criterion, the adjusted major error rate was 2.4%. Overall, performance is acceptable.

When evaluating results by individual species, for *K. pneumoniae* group, the EA was 97.4% and the CA was 100%. There were no minor, five (5) major (7.1%) and no very major errors. The following statement is included as a limitation in the device labeling to address the major errors:

Due to the occurrence of a major errors with cefuroxime, isolates of *K. pneumoniae* group that provide a MIC of 16 µg/mL should be retested by an alternate method.

For *K. oxytoca,* the EA was 97.5% and the CA was 90%. There were no minor, four (4) major (14.8%) errors and no very major errors. The following statement is included as a limitation in the device labeling to address the major errors:

Due to the occurrence of a major errors with cefuroxime, isolates of *K. oxytoca* that provide a MIC of 32 µg/mL should be retested by an alternate method.

For *C. koseri,* the EA was 92.6% and the CA was 96.3%. There were no minor, one (1) major (4.3%) error and no very major errors. The following statement is included as a limitation in the device labeling to address the major error:

Due to the occurrence of a major error with cefuroxime, isolates of *C. koseri* that provide a MIC of > 32 µg/mL should be retested by an alternate method.

Ciprofloxacin. A total of 751 specimens (303 *E. coli,* 123 *K. pneumoniae* group*,* 46 *K. oxytoca,* 47 *K. aerogenes,* 39 *E. cloacae* complex*,* 26 *C. freundii* complex*,* 38 *P. mirabilis,* 33 *P. vulgaris,* 26 *S. marcescens* and 70 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 99.0% and CA of 95.6%. There were 28 minor (4.1%), one (1) major (0.2%) error and one (1) very major (0.5%) error. Overall, performance is acceptable.

For *P. mirabilis*, the EA was 97.4% and the CA was 94.7%. There were one (1) minor (2.6%) error, no major and one (1) very major (5.0%) error. The following statement is included as a limitation in the device labeling to address the very major error:

Due to the occurrence of a very major error with ciprofloxacin, isolates of *P. mirabilis* that provide a MIC of 0.25 µg/mL should be retested by an alternate method.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 92.9% and CA of 97.1%, which is acceptable. There were one (1) minor (1.4%) error, one (1) major (3.0%) error and no very major errors. Overall, performance is acceptable.

Ertapenem. A total of 493 specimens (301 *E. coli*, 126 *K. pneumoniae* group, 40 *P. mirabilis*, and 26 *P. vulgaris*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 97.8% and CA of 98.8%. There were five (5) minor (1.0%), one (1) major (0.2%) and no very major errors. Overall, performance is acceptable.

Gentamicin. A total of 749 specimens (299 *E. coli,* 123 *K. pneumoniae group,* 40 *K. oxytoca,* 46 *K. aerogenes,* 30 *C. freundii* complex*,* 35 *C. koseri,* 30 *P. mirabilis,* 55 *P. vulgaris,* 26 *S. marcescens* and 65 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 96.6% and CA of 98.2%. There were nine (9) minor (1.3%) errors, two (2) major (0.3%) errors and one (1) very major (1.0%) error. Overall, performance is acceptable.

When evaluating results by individual species, for *E. coli* the EA was 97.3% and the CA was 98.3%. There were two (2) minor (0.7%) errors, two (2) major (0.8%) errors and one (1) very

major (2.3%) error. The following statement is included as a limitation in the device labeling to address the very major error:

> Due to the occurrence of a very major error with gentamicin, isolates of *E. coli* that provide a MIC of 4 µg/mL should be retested by an alternate method.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 96.9% and CA of 95.4%, which is acceptable. There were three (3) minor (4.6%) errors, no major and no very major errors. Overall, performance is acceptable.

Imipenem. A total of 682 specimens (301 *E. coli,* 124 *K. pneumoniae* group*,* 44 *K. oxytoca,* 39 *E. cloacae* complex*,* 38 *C. koseri,* 26 *S. marcescens*, 45 *A. baumannii-calcoaceticus*, and 65 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 98.1% and CA of 97.7%. There were 13 minor (2.3%) errors, no major and no very major errors. Overall, performance is acceptable.

The *A. baumannii-calcoaceticus* results from clinical and challenge testing demonstrated an EA of 97.8% and CA of 93.3%. There were three (3) minor (6.7%) errors, no major and no very major errors. Overall, performance is acceptable.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 93.8% and CA of 93.8%. There were two (2) minor (3.1%) errors, no major and two (2) very major (4.9%) errors. The following statement is included as a limitation in the device labeling to address the very major errors:

> Due to the occurrence of very major errors with imipenem, isolates of *P. aeruginosa* that provide a MIC of 2 µg/mL should be retested by an alternate method.

Levofloxacin. A total of 798 specimens (300 *E. coli,* 124 *K. pneumoniae* group*,* 44 *K. oxytoca,* 47 *K. aerogenes,* 39 *E. cloacae* complex*,* 31 *C. freundii* complex*,* 37 *C. koseri,* 31 *P. mirabilis,* 36 *P. vulgaris,* 35 *S. marcescens* and 74 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 99.2% and CA of 96.3%. There were 26 minor (3.6%) errors, no major and one (1) very major (0.5%) error. Overall, performance is acceptable.

When evaluating results by individual species, for *P. mirabilis* the EA was 93.5% and the CA was 96.8%. There were no minor, no major and one (1) very major (6.7%) error. The following statement is included as a limitation in the device labeling to address the very major error:

> Due to the occurrence of a very major error with levofloxacin, isolates of *P. mirabilis* that provide a MIC of 0.5 µg/mL should be retested by an alternate method.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 97.3% and CA of 94.6%. There were three (3) minor (4.1%) errors, one (1) major (2.9%) errors and no very major errors. Overall, performance is acceptable.

Meropenem. A total of 738 specimens (301 *E. coli,* 123 *K. pneumoniae* group*,* 39 *E. cloacae* complex*,* 50 *P. mirabilis,* 59 *P. vulgaris,* 40 *S. marcescens*, 61 *A. baumannii-calcoaceticus*

complex, and 65 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 97.2% and CA of 98.5%. There were six (6) minor (1.0%) errors, three (3) major (0.6%) errors and no very major errors. Overall, performance is acceptable.

The *A. baumannii-calcoaceticus* complex results from clinical and challenge testing demonstrated an EA of 90.2% and CA of 96.7%. There were two (2) minor (3.3%) errors, no major and no very major errors. Overall, performance is acceptable.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 96.9%and CA of 92.3%. There were five (5) minor (7.7%) errors, no major and no very major errors. Overall, performance is acceptable.

Meropenem/Vaborbactam. A total of 692 specimens (298 *E. coli*, 123 *K. pneumoniae* group, 45 *K. oxytoca*, 47 *K. aerogenes*, 43 *E. cloacae* complex, 36 *C. freundii* complex, 61 *C. koseri*, and 39 *P. mirabilis*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 97.1% and CA of 98.0%. There were 14 minor (2.0%) errors, no major and no very major errors. Overall, performance is acceptable.

Piperacillin/Tazobactam. A total of 489 specimens (299 *E. coli*, 122 *K. pneumoniae* group, 33 *C. koseri*, and 35 *P. vulgaris*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 94.7% and CA of 94.9%. There were 20 minor (4.1%) errors, four (4) major (1.0%) errors and one (1) very major (1.4%) error. Overall, performance is acceptable.

When evaluating results by individual species, *C. koseri* demonstrated an EA of 97.0% and the CA of 87.9%. There were four (4) minor (12.1%) errors, no major and no very major errors. According to the AST Special Controls document, a CA <90.0% caused by a high number of minor errors is acceptable when very good EA of evaluable results are observed. The EA of evaluable results was 90.9%. Performance is acceptable.

For *E. coli,* the EA was 95.3% and the CA was 95.3%. There were 11 minor (3.7%) errors, two (2) major (0.8%) errors and one (1) very major (3.3%) errors. The following statement is included as a limitation in the device labeling to address the very major error:

> Due to the occurrence of a very major error with piperacillin/tazobactam, isolates of *E. coli* that provide a MIC of 8 µg/mL should be retested by an alternate method.

Tetracycline. A total of 552 specimens (301 *E. coli,* 123 *K. pneumoniae* group*,* 42 *K. oxytoca,* 47 *K. aerogenes* and 39 *A. baumannii-calcoaceticus* complex) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 98.4% and CA of 97.1%. There were 12 minor (2.3%) errors, three (3) major (0.8%) errors and no very major errors. Overall, performance is acceptable.

When evaluating results by individual species, *K. aerogenes* demonstrated an EA of 97.9% and the CA of 87.2%. There were six (6) minor (12.8%) errors, no major and no very major errors. According to the AST Special Controls document, a CA <90.0% caused by a high number of minor errors is acceptable when very good EA of evaluable results are observed. The EA of evaluable results was 96.2%. Performance is acceptable.

The *A. baumannii-calcoaceticus* complex results from clinical and challenge testing demonstrated an EA of 100% and CA of 100%. There were no minor, no major and no very major errors. Overall, performance is acceptable.

Tobramycin. A total of 722 specimens (300 *E. coli,* 124 *K. pneumoniae* group*,* 40 *K. oxytoca,* 46 *K. aerogenes,* 39 *E. cloacae* complex*,* 22 *C. freundii* complex*,* 29 *C. koseri,* 31 *P. mirabilis,* 26 *S. marcescens* and 65 *P. aeruginosa*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 96.5% and CA of 94.8%. There were 30 minor (4.6%) errors, one (1) major (0.2%) error and three (3) very major (2.8%) errors. Overall, performance is acceptable.

When evaluating results by individual species, for *E. coli* the EA was 97.7% and the CA was 93.7%. There were 17 minor (5.6%) error, no major and two (2) very major (5.1%) errors. The following statement is included as a limitation in the device labeling to address the very major errors:

> Due to the occurrence of very major errors with tobramycin, isolates of *E. coli* that provide a MIC of 4 µg/mL should be retested by an alternate method.

For *K. oxytoca,* the EA was 97.5% and the CA was 90%. There were three (3) minor (7.5%) errors, no major and one (1) very major (20.0%) error. The one (1) very major error was considered a random error due to the limited number of resistant isolates tested. This performance is acceptable.

For *S. marcescens,* the EA was 92.3% and the CA was 92.3%. There were one (1) minor (3.8%) error, one (1) major (4.2%) error and no very major errors. The following statement is included as a limitation in the device labeling to address the major error:

> Tobramycin with *S. marcescens* may produce a resistant result that can be found susceptible by the reference method. If critical to patient care, confirm these results with an alternate method.

The *P. aeruginosa* results from clinical and challenge testing demonstrated an EA of 100% and CA of 100%. There were no minor, no major and no very major errors. Overall, performance is acceptable.

Trimethoprim/sulfamethoxazole. A total of 482 specimens (303 *E. coli*, 130 *K. pneumoniae* group, and 47 *K. aerogenes*) were evaluated. The Enterobacterales results from clinical and challenge testing demonstrated an EA of 95.0% and CA of 96.5%. There were no minor, 14 major (4.3%) errors and three (3) very major (1.9%) errors. Overall, performance is acceptable.

When evaluating results by individual species, for *E. coli* the EA was 93.4% and the CA was 95.4%. There were no minor, 12 major (5.8%) errors and two (2) very major (2.1%) errors. Based on the AST Special Controls, the very major error rate is acceptable due to the high number of resistant *E. coli* isolates tested (2/95 = 2.1%). To address the major errors, the following statement is included as a limitation in the device labeling:

Due to the occurrence of major errors with trimethoprim/sulfamethoxazole, isolates of *E. coli* that provide a MIC of 4-64 µg/mL should be retested by an alternate method.

ESBL. A total of 408 specimens were evaluated (*E. coli, K. pneumoniae* group, and *K. oxytoca*). The Enterobacterales results demonstrated an CA of 98.5%. The ESBL screen is for the detection of organisms that produce extended spectrum beta lactamase and generates a "Positive" or "Negative" result; therefore, EA was not calculated. There were five (5) major and one (1) very major error (1.3%). Two of the major errors were due to *K. oxytoca* and are addressed by the following limitation in the device labeling:

Isolates of *K. oxytoca* that test as ESBL positive should be retested by an alternate method to confirm the presence of ESBL.

As required under 511A(b)(2)(C)(ii)(I) of the Federal Food, Drug and Cosmetic Act, the following statement was added to the package insert to address testing of non-indicated species:

Per the FDA-Recognized Susceptibility Test Interpretive Criteria website, 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.

Table 9. VITEK REVEAL AST System – GN Panel Performance

Sample Type	Total	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R/NS	No. S	min	major	vmj
Amikacin: Enterobacterales [Breakpoints (µg/mL): 16 (S), 32 (I), 64 (R)]													
Clinical	443	434	98.0	421	412	97.7	442	99.8	1	441	1	0	0
Challenge	188	185	98.4	147	143	97.9	185	98.4	37	147	3	0	0
Combined	631	619	98.1	567	555	97.9	627	99.4	38	588	4	0	0
Amikacin: *A. baumannii-calcoaceticus* complex [Breakpoints (µg/mL): 16 (S), 32 (I), 64 (R)]													
Clinical	13	9	69.2	12	8	66.7	12	92.3	2	11	1	0	0
Challenge	47	45	95.7	37	35	94.6	41	87.2	13	29	6	0	0
Combined	60	54	90.0	49	43	87.8	53	88.3	15	40	7	0	0
Amikacin: *P. aeruginosa* [Breakpoints (µg/mL): 16 (S), 32 (I), 64 (R)]													
Clinical	27	26	96.3	26	25	96.2	27	100	0	27	0	0	0
Challenge	38	36	94.7	24	22	97.7	35	92.1	24	11	3	0	0
Combined	65	62	95.4	50	47	94.0	62	95.4	24	38	3	0	0
Amoxicillin/Clavulanate: Enterobacterales [Breakpoints (µg/mL): 8 (S), 16 (I), 32 (R)]													
Clinical	370	361	97.6	156	147	94.2	338	91.4	8	347	29	3	0
Challenge	130	114	87.7	67	51	76.1	116	89.2	59	61	14	0	0
Combined	500	475	95.0	223	198	88.8	454	90.8	67	408	43	3	0
Ampicillin/Sulbactam: Enterobacterales [Breakpoints (µg/mL): 8 (S), 16 (I), 32 (R)]													
Clinical	287	287	97.9	142	136	95.8	220	76.7	25	222	66	1	0
Challenge	86	84	97.7	39	37	94.9	68	79.1	40	31	16	2	0
Combined	372	364	97.8	181	173	95.6	287	77.2*	65	252	82	3	0
Aztreonam: Enterobacterales [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													

Sample Type	Total	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R/NS	No. S	min	major	vmj
Clinical	374	366	97.9	55	47	85.5	368	97.3	51	314	8	2	0
Challenge	156	150	96.2	38	32	84.2	145	92.9	90	58	10	1	0
Combined	530	516	97.4	93	79	84.9	543	96.0	141	372	18	3	0
Aztreonam: *P. aeruginosa* [Breakpoints (µg/mL): 8 (S), 16 (I), 32 (R)]													
Clinical	27	26	96.3	26	25	96.2	25	92.6	4	23	2	0	0
Challenge	38	37	97.4	25	24	96.0	31	81.6	18	14	7	0	0
Combined	65	63	96.9	51	49	96.1	56	86.2*	22	37	9	0	0
Cefepime: Enterobacterales [Breakpoints (µg/mL): 2 (S), 4-8 (SDD^), 16 (R)]													
Clinical	397	384	96.7	52	39	75.0	384	96.7	42	344	11	2	0
Challenge	182	172	94.5	64	54	84.4	171	94.0	77	88	10	1	0
Combined	579	556	96.0	116	93	80.2	555	95.9	119	432	21	3	0
Cefepime: *P. aeruginosa* [Breakpoints (µg/mL): 8 (S), - (I), 16 (R)]													
Clinical	28	26	92.9	28	26	92.9	27	96.4	2	26	n/a	1	0
Challenge	38	38	100.0	18	18	100.0	37	97.4	31	7	n/a	1	0
Combined	66	64	97.0	46	44	95.7	64	97.0	33	33	n/a	2	0
Cefotaxime: Enterobacterales [Breakpoints (µg/mL): 1 (S), 2 (I), 4 (R)]													
Clinical	381	374	98.2	24	17	70.8	379	99.5	68	313	2	0	0
Challenge	173	165	95.4	42	34	81.0	170	98.3	115	56	1	2	0
Combined	554	539	97.3	66	51	77.3	549	99.1	183	369	3	2	0
Cefotaxime: *A. baumannii-calcoaceticus* complex [Breakpoints (µg/mL): 1 (S), 2 (I), 4 (R)]													
Clinical	13	13	100.0	9	9	100.0	13	100.0	13	0	0	0	0
Challenge	25	25	100.0	5	5	100.0	25	100.0	25	0	0	0	0
Combined	38	38	100.0	14	14	100.0	38	100.0	38	0	0	0	0
Ceftazidime: Enterobacterales [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	398	381	95.7	118	101	85.6	384	96.5	51	339	13	1	0
Challenge	182	172	94.5	57	47	82.5	179	98.4	106	74	3	0	0
Combined	580	553	95.3	175	148	84.6	563	97.1	157	413	16	1	0
Ceftazidime: *A. baumannii-calcoaceticus* complex [Breakpoints (µg/mL): 8 (S), 16 (I), 32 (R)]													
Clinical	13	12	92.3	9	8	88.9	12	92.3	4	9	1	0	0
Challenge	26	26	100.0	12	12	100.0	25	96.2	21	3	1	0	0
Combined	39	38	97.4	21	20	95.2	37	94.9	25	12	2	0	0
Ceftazidime/Avibactam: Enterobacterales [Breakpoints (µg/mL): 8 (S), - (I), 16 (R)]													
Clinical	421	408	96.9	176	163	92.6	420	99.8	1	420	n/a	1	0
Challenge	203	189	93.7	126	112	88.9	202	99.5	53	150	n/a	0	1
Combined	624	597	95.7	302	275	91.1	692	99.7	54	570	n/a	1	1
Ceftazidime/Avibactam: *P. aeruginosa* [Breakpoints (µg/mL): 8 (S), - (I), 16 (R)]													
Clinical	28	28	100.0	27	27	100.0	28	100.0	1	27	n/a	0	0
Challenge	65	63	96.9	44	42	95.5	63	96.9	26	39	n/a	2	0
Combined	93	91	97.8	71	69	97.2	91	97.8	27	66	n/a	2	0
Ceftolozane/Tazobactam: Enterobacterales [Breakpoints (µg/mL): 2 (S), 4 (I), 8 (R)]													
Clinical	346	313	90.5	321	288	89.7	339	98.0	8	336	5	1	1
Challenge	164	161	98.2	127	124	97.6	159	97.0	59	100	5	0	0
Combined	510	474	92.9	448	412	92.0	498	97.6	67	436	10	1	1
Ceftolozane/Tazobactam: *P. aeruginosa* [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	28	28	100.0	28	28	100.0	27	96.4	0	27	1	0	0
Challenge	38	38	100.0	10	10	100.0	38	100.0	28	10	0	0	0
Combined	66	66	100.0	38	38	100.0	65	98.5	28	37	1	0	0

Sample Type	Total	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R/NS	No. S	min	major	vmj
Ceftriaxone: Enterobacterales [Breakpoints (µg/mL): 1 (S), 2 (I), 4 (R)]													
Clinical	394	390	99.0	10	6	60.0	392	99.5	65	326	1	1	0
Challenge	232	218	94.0	48	34	70.8	213	91.8	135	79	17	2	0
Combined	626	608	97.1	58	40	69.0	605	96.6	200	405	18	3	0
Cefuroxime: Enterobacterales [Breakpoints (µg/mL): 8 (S), - (I), 16 (R)]													
Clinical	384	368	95.8	274	258	94.2	374	97.4	68	316	n/a	9	1
Challenge	138	132	95.7	60	54	90.0	134	97.1	81	57	n/a	4	0
Combined	522	500	95.8	334	312	93.4	508	97.3	149	373	n/a	13	1
Ciprofloxacin: Enterobacterales [Breakpoints (µg/mL): 0.25 (S), 0.5 (I), 1 (R)]													
Clinical	464	461	99.4	60	57	95.0	448	96.6	92	367	16	0	0
Challenge	217	213	98.2	62	58	93.5	203	93.5	109	96	12	1	1
Combined	681	674	99.0	122	115	94.3	651	95.6	201	463	28	1	1
Ciprofloxacin: *P. aeruginosa* [Breakpoints (µg/mL): 0.5 (S), 1 (I), 2 (R)]													
Clinical	28	23	82.1	14	9	64.3	26	92.9	2	25	1	1	0
Challenge	42	42	100.0	4	4	100.0	42	100.0	34	8	0	0	0
Combined	70	65	92.9	18	13	72.2	68	97.1	36	33	1	1	0
Ertapenem: Enterobacterales [Breakpoints (µg/mL): 0.5 (S), 1 (I), 2 (R)]													
Clinical	368	363	98.6	12	7	58.3	366	99.5	5	361	1	1	0
Challenge	125	119	95.2	16	10	62.5	121	96.8	62	61	4	0	0
Combined	493	482	97.8	28	17	60.7	487	98.8	67	422	5	1	0
Gentamicin: Enterobacterales [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	458	445	97.2	316	302	95.9	453	98.9	38	419	3	1	1
Challenge	226	216	95.6	123	113	91.9	219	96.9	61	159	6	1	0
Combined	684	661	96.6	438	415	94.7	672	98.2	99	578	9	2	1
Gentamicin: *P. aeruginosa* [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	27	27	100.0	26	26	100.0	26	96.3	0	25	1	0	0
Challenge	38	36	94.7	14	12	85.7	36	94.7	27	7	2	0	0
Combined	65	63	96.9	40	38	95.0	62	95.4	27	32	3	0	0
Imipenem: Enterobacterales [Breakpoints (µg/mL): 1 (S), 2 (I), 4 (R)]													
Clinical	402	397	98.8	41	36	87.8	400	99.5	5	395	2	0	0
Challenge	170	164	96.5	55	49	89.8	159	93.5	68	92	11	0	0
Combined	572	561	98.1	96	85	88.5	559	97.7	73	487	13	0	0
Imipenem: *A. baumannii-calcoaceticus* complex [Breakpoints (µg/mL): 2 (S),42 (I),84 (R)]													
Clinical	13	12	92.3	2	1	50.0	12	92.3	5	8	1	0	0
Challenge	32	32	100.0	8	8	100.0	30	93.8	21	7	2	0	0
Combined	45	44	97.8	10	9	90.0	42	93.3	26	15	3	0	0
Imipenem: *P. aeruginosa* [Breakpoints (µg/mL): 2 (S), 4 (I), 8 (R)]													
Clinical	27	24	88.9	26	23	88.5	23	85.2	4	21	2	0	2
Challenge	38	37	97.4	9	8	88.9	38	100.0	37	1	0	0	0
Combined	65	61	93.8	35	31	88.6	61	93.8	41	22	2	0	2
Levofloxacin: Enterobacterales [Breakpoints (µg/mL): 0.5 (S), 1 (I), 2 (R)]													
Clinical	481	476	99.0	105	100	95.2	469	97.5	88	385	11	0	1
Challenge	243	242	99.6	93	92	98.9	228	93.8	109	115	15	0	0
Combined	724	718	99.2	198	192	97.0	697	96.3	197	500	26	0	1
Levofloxacin: *P. aeruginosa* [Breakpoints (µg/mL): 1 (S), 2 (I), 4 (R)]													
Clinical	28	27	96.4	25	24	96.0	26	92.9	2	24	1	1	0
Challenge	46	45	97.8	14	13	92.9	44	95.7	35	10	2	0	0

Sample Type	Total	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R/NS	No. S	min	major	vmj
Combined	74	72	97.3	39	37	94.9	70	94.6	37	34	3	1	0
Meropenem: Enterobacterales [Breakpoints (µg/mL): 1 (S), 2 (I), 4 (R)]													
Clinical	406	399	98.3	19	12	63.2	4.0	99.3	4	402	1	2	0
Challenge	206	196	35.1	72	62	86.1	200	97.1	71	132	5	1	0
Combined	612	595	97.2	91	74	81.3	603	98.5	75	534	6	3	0
Meropenem: *A. baumannii-calcoaceticus* complex [Breakpoints (µg/mL): 2 (S),4 (I),8 (R)]													
Clinical	13	12	92.3	10	9	90.0	13	100.0	5	8	0	0	0
Challenge	48	43	89.6	31	26	83.9	46	95.8	25	21	2	0	0
Combined	61	55	90.2	41	35	85.4	59	96.7	30	29	2	0	0
Meropenem: *P. aeruginosa* [Breakpoints (µg/mL): 2 (S), 4 (I), 8 (R)]													
Clinical	27	26	96.3	26	25	96.2	25	92.6	1	24	2	0	0
Challenge	38	37	97.4	16	15	93.8	35	92.1	30	3	3	0	0
Combined	65	63	96.9	42	40	95.2	60	92.3	31	27	5	0	0
Meropenem/Vaborbactam: Enterobacterales [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	437	432	98.9	10	5	50.0	436	99.8	1	436	1	0	0
Challenge	255	240	94.1	80	65	81.2	242	94.9	52	199	13	0	0
Combined	692	672	97.1	90	70	77.8	678	98.0	53	635	14	0	0
Piperacillin/Tazobactam: Enterobacterales [Breakpoints (µg/mL): 8 (S), 16 (I), 32 (R)]													
Clinical	358	336	93.9	46	24	52.2	344	96.1	13	338	10	3	1
Challenge	131	127	97.0	28	24	85.7	120	91.6	59	63	10	1	0
Combined	489	463	94.7	74	48	64.9	464	94.9	72	401	20	4	1
Tetracycline: Enterobacterales [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	365	359	98.4	112	106	94.6	359	98.4	81	281	3	3	0
Challenge	148	146	98.6	77	75	97.4	139	93.9	69	75	9	0	0
Combined	513	505	98.4	189	181	95.8	498	97.1	150	356	12	3	0
Tetracycline: *A. baumannii-calcoaceticus* complex [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	13	13	100.0	6	6	100.0	13	100.0	5	6	0	0	0
Challenge	26	26	100.0	4	4	100.0	26	100.0	25	1	0	0	0
Combined	39	39	100.0	10	10	100.0	39	100.0	30	7	0	0	0
Tobramycin: Enterobacterales [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	462	445	96.3	458	441	96.3	437	94.6	31	420	22	1	2
Challenge	195	189	96.9	150	144	96.0	186	95.4	78	112	8	0	1
Combined	657	634	96.5	608	585	96.2	623	94.8	109	532	30	1	3
Tobramycin: *P. aeruginosa* [Breakpoints (µg/mL): 4 (S), 8 (I), 16 (R)]													
Clinical	27	27	100.0	27	27	100.0	27	100.0	0	27	0	0	0
Challenge	38	38	100.0	8	8	100.0	38	100.0	31	7	0	0	0
Combined	65	65	100.0	35	35	100.0	65	100.0	31	34	0	0	0
Trimethoprim/Sulfamethoxazole: Enterobacterales [Breakpoints (µg/mL): 2 (S), - (I), 4 (R)]													
Clinical	338	326	96.5	15	3	20.0	331	97.9	80	258	n/a	5	2
Challenge	142	130	91.5	23	11	47.8	132	93.0	75	67	n/a	9	1
Combined	480	456	95.0	38	14	36.8	463	96.5	155	325	n/a	14	3

EA – Essential Agreement
CA – Category Agreement
EVAL – Evaluable isolates
R – Resistant isolates
N – Non-susceptible isolates
S – Susceptible isolates
min – minor errors
maj – major errors
vmj – very major errors

Essential Agreement (EA) occurs when there is agreement between the reference method and VITEK REVEAL MIC results within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on-scale for both the VITEK REVEAL and the

reference method or those in which an off-scale result is at least two doubling dilutions from the on-scale result. Category Agreement (CA) occurs when the interpretation of the reference method and VITEK REVEAL result are in exact agreement.

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

* Low category agreement was due to the occurrence of a high number of minor errors for the following: ampicillin-sulbactam/Enterobacterales; aztreonam/*P. aeruginosa*

Table 10. VITEK REVEAL AST System – ESBL

Sample Type	Total	No. CA	CA %	POS	NEG	major	vmj
E. coli, *K. pneumoniae* group, and *K. oxytoca*							
Clinical	340	338	99.4	53	287	1	1
Challenge	68	64	94.1	19	49	4	0
Combined	408	402	98.5	72	336	5	1

Trending Analysis

A trending analysis using combined clinical and challenge isolate results was also conducted to evaluate antimicrobial-organism combinations for which VITEK REVEAL MIC results were determined to be one or more doubling dilutions lower or higher than the reference result. MIC results that were off scale for both the reference and VITEK REVEAL 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 ≥ 30% with a statistically significant confidence interval were considered to have evidence of trending and is addressed in the labeling (**Table 11**).

Analysis of trending indicated that VITEK REVEAL MIC values for certain antimicrobial/organism combinations tended to be at least one doubling dilution lower than the reference MIC value. The following statement is included as a footnote to the AST performance table:

VITEK REVEAL MIC values for the following antimicrobial/organism combinations tended to be one doubling dilution lower than the reference MIC value:

- Amikacin: *C. freundii* complex, *K. oxytoca*, and *P. aeruginosa*
- Aztreonam: *K. oxytoca* and *P. aeruginosa*
- Ceftazidime: *C. koseri*, *E. coli*, *K. aerogenes*, *K. oxytoca*, and *K. pneumoniae* group
- Ceftazidime/Avibactam: All Enterobacterales except for *E. cloacae* complex
- Cefotaxime: *K. aerogenes* and *A. baumannii-calcoaceticus* complex
- Ceftolozane/Tazobactam: *E. coli*, *K, aerogenes*, *K. oxytoca, P. aeruginosa*
- Cefuroxime: *C. koseri*, *E. coli*, and *P. mirabilis*
- Ertapenem: *E. coli*
- Imipenem: *E. cloacae* complex, *A. baumannii-calcoaceticus* complex, and *P. aeruginosa*
- Levofloxacin: *K. pneumoniae* group*, K. aerogenes, E, cloacae* complex*, C. freundii* complex*,* and *P. mirabilis*
- Meropenem: *A. baumannii-calcoaceticus* complex, *P. aeruginosa* and *S. marcescens*

- Meropenem/Vaborbactam: *C. freundii* complex, *K. pneumoniae* group, and *K. aerogenes*
- Piperacillin/Tazobactam: *C. koseri*, *E. coli,* and *K. pneumoniae* group
- Tetracycline: *K. aerogenes*
- Tobramycin: *P. mirabilis*

VITEK REVEAL MIC values for the following antimicrobial/organism combinations tended to be one doubling dilution higher than the reference MIC value:

- Amikacin: *S. marcescens*
- Amoxicillin/Clavulanate: *E. coli, K. pneumoniae* group and *P. mirabilis*
- Ampicillin/Sulbactam: *E. coli*
- Aztreonam: *E. coli*
- Cefepime: *E. cloacae* complex
- Cefotaxime: *E. coli* and *K. pneumoniae* group
- Ceftazidime: *A. baumannii-calcoaceticus* complex
- Ceftriaxone: *K. pneumoniae* group
- Cefuroxime: *K. pneumoniae* group
- Ciprofloxacin: *C. freundii* complex, *C. koseri, E. cloacae* complex, *E. coli, K. pneumoniae* group, and *S. marcescens*
- Gentamicin: *C. freundii* complex, *E. coli, K. aerogenes, K. pneumoniae* group, and *S. marcescens*
- Imipenem: *E. coli* and *K. pneumoniae* group
- Levofloxacin: *P. aeruginosa*
- Meropenem: *P. mirabilis*
- Meropenem/Vaborbactam: *C. koseri* and *P. mirabilis*
- Tobramycin: *E. cloacae* complex and *C. freundii* complex
- Trimethoprim/sulfamethoxazole: *E. coli* and *K. pneumoniae* group

Table 11. VITEK REVEAL AST System – GN Panel Trending

Drug	Organism Name	Total On Scale for Trending	≥ 1 Dilution Lower # (%)	Exact #	≥ 1 Dilution Higher # (%)	Percent Difference (95% CI)	Statistically Significant Trending Noted
Amikacin	*A. baumannii-calcoaceticus* complex	52	23, (44.2)	19	10, (19.2)	-25%, (-40.9%, -7.1%)	No
	Citrobacter freundii complex	21	13, (61.9)	8	0, (0)	-62%, (-79%, -36%)	Yes
	Enterobacter cloacae complex	36	10, (27.8)	24	2, (5.6)	-22.2%, (-38.9%, 4.9%)	No
	Escherichia coli	291	76, (26.12)	173	42, (14.4)	-12%, (-18%, -5%)	No
	Klebsiella aerogenes	46	12, (26.09)	29	5, (10.9)	-15%, (-31%, 1%)	No
	Klebsiella oxytoca	38	16, (42.11)	21	1, (2.6)	-39%, (-55%, -22%)	Yes

Drug	Organism Name	Total On Scale for Trending	≥ 1 Dilution Lower # (%)	Exact #	≥ 1 Dilution Higher # (%)	Percent Difference (95% CI)	Statistically Significant Trending Noted
	Klebsiella pneumoniae group	101	20, (19.8)	78	3, (3.0)	-17%, (-26%, -8%)	No
	Proteus mirabilis	31	14, (45.16)	11	6, (19.4)	-26%, (-46%, -3%)	No
	Serratia marcescens	26	0, (0)	4	22, (84.6)	85%, (62%, 94%)	Yes
	Pseudomonas aeruginosa	57	25, (43.9)	26	6, (10.5)	-33%, (-47%, -17%)	Yes
Amoxicillin/ Clavulanate	*Escherichia coli*	218	4, (1.8)	52	162, (74.31)	72%, (66%, 78%)	Yes
	Klebsiella oxytoca	11	1, (9.1)	6	4, (36.36)	27%, (-8%, 56%)	No
	Klebsiella pneumoniae group	56	0, (0)	13	43, (76.79)	77%, (63%, 86%)	Yes
	Proteus mirabilis	11	0, (0)	7	4, (36.36)	36%, (3%, 65%)	Yes
Ampicillin/ Sulbactam	*Escherichia coli*	156	21, (13.5)	45	90, (57.69)	44%, (34%, 53%)	Yes
	Klebsiella oxytoca	33	14, (42.4)	10	9, (27.27)	-15%, (-36%, 8%)	No
	Proteus mirabilis	11	3, (27.3)	5	3, (27.27)	0%, (-34%, 34%)	No
Aztreonam	*Citrobacter freundii* complex	10	5, (50)	1	4, (40)	-10%, (-45%, 29%)	No
	Enterobacter cloacae complex	18	4, (22.2)	9	5, (27.8)	6%, (-22%, 32%)	No
	Escherichia coli	54	10, (18.5)	18	26, (48.15)	30%, (12%, 45%)	Yes
	Klebsiella oxytoca	17	10, (58.8)	4	3, (17.65)	-41%, (-64%, -9%)	Yes
	Klebsiella pneumoniae group	14	4, (28.6)	3	7, (50)	21%, (-13%, 50%)	No
	Pseudomonas aeruginosa	53	21, (39.6)	30	2, (3.8)	-36%, (-50%, -21%)	Yes
Cefepime	*Citrobacter koseri*	12	6, (50)	4	2, (16.7)	-33%, (-61%, 4%)	No
	Enterobacter cloacae complex	19	2, (10.5)	6	11, (57.9)	47%, (17%, 68%)	Yes
	Escherichia coli	48	17, (35.42)	16	15, (31.25)	-4%, (-22%, 14%)	No
	Klebsiella aerogenes	25	6, (24)	8	11, (44)	20%, (-6%, 43%)	No
	Klebsiella oxytoca	12	3, (25)	5	4, (33.33)	8%, (-26%, 40%)	No
	Klebsiella pneumoniae group	22	6, (27.27)	6	10, (45.45)	18%, (-10%, 43%)	No
	Pseudomonas aeruginosa	46	10, (21.74)	27	9, (19.57)	-2%, (-19%, 14%)	No
Cefotaxime	*Acinetobacter baumannii* complex	21	10, (47.62)	11	0, (0)	-48%, (-68%, -23%)	Yes
	Enterobacter cloacae complex	12	1, (8.33)	6	5, (41.67)	33%, (-2%, 61%)	No
	Escherichia coli	29	4, (13.79)	8	17, (58.62)	45%, (20%, 63%)	Yes

Drug	Organism Name	Total On Scale for Trending	≥ 1 Dilution Lower # (%)	Exact #	≥ 1 Dilution Higher # (%)	Percent Difference (95% CI)	Statistically Significant Trending Noted
	Klebsiella aerogenes	25	18, (72)	7	0, (0)	-72%, (-86%, -48%)	Yes
	Klebsiella oxytoca	10	3, (30)	5	2, (20)	-10%, (-44%, 26%)	No
	Klebsiella pneumoniae group	10	0, (0)	2	8, (80)	80%, (38%, 94%)	Yes
Ceftazidime	*Acinetobacter baumannii* complex	22	1, (4.55)	11	10, (45.45)	41%, (16%, 61%)	Yes
	Citrobacter koseri	21	18, (85.71)	3	0, (0)	-86%, (-95%, -60%)	Yes
	Enterobacter cloacae complex	19	5, (26.32)	8	6, (31.58)	5%, (-22%, 32%)	No
	Escherichia coli	184	108, (58.7)	38	38, (20.65)	-38%, (-47%, -28%)	Yes
	Klebsiella aerogenes	36	24, (66.67)	9	3, (8.33)	-58%, (-73%, -37%)	Yes
	Klebsiella oxytoca	16	8, (50)	8	0, (0)	-50%, (-72%, -21%)	Yes
	Klebsiella pneumoniae group	55	32, (58.18)	13	10, (18.18)	-40%, (-54%, -22%)	Yes
Ceftazidime/ Avibactam	*Citrobacter freundii* complex	16	11, (68.75)	2	3, (18.75)	-50%, (-71%, -16%)	Yes
	Citrobacter koseri	17	11, (64.71)	3	3, (17.65)	-47%, (-68%, -14%)	Yes
	Enterobacter cloacae complex	34	6, (17)	23	5, (15)	-2.9%, (-21%, 15%)	No
	Escherichia coli	213	142, (66.67)	66	5, (2.35)	-64%, (-70%, -57%)	Yes
	Klebsiella aerogenes	58	36, (62.07)	19	3, (5.17)	-57%, (-69%, -41%)	Yes
	Klebsiella pneumoniae group	93	20, (53.8)	38	5, (5.4)	-48%, (-59%, -36%)	Yes
	Proteus mirabilis	13	10, (76.92)	3	0, (0)	-77%, (-92%, -41%)	Yes
	Pseudomonas aeruginosa	76	22, (28.95)	45	9, (11.84)	-17%, (-29%, -4%)	No
Ceftolozane/ Tazobactam	*Citrobacter koseri*	42	15, (35.71)	19	8, (19.05)	-17%, (-34%, 2%)	No
	Enterobacter cloacae complex	29	5, (17.2)	14	10, (34.5)	17%, (-5%, 39%)	No
	Escherichia coli	273	180, (65.93)	87	6, (2.2)	-64%, (-69%, -57%)	Yes
	Klebsiella aerogenes	43	26, (60.47)	12	5, (11.63)	-49%, (-64%, -29%)	Yes
	Klebsiella oxytoca	39	24, (61.54)	14	1, (2.56)	-59%, (-73%, -40%)	Yes
	Proteus mirabilis	31	4, (12.9)	22	5, (16.13)	3%, (-15%, 21%)	No
	Proteus vulgaris	22	1, (4.55)	19	2, (9.09)	5%, (-14%, 24%)	No

Drug	Organism Name	Total On Scale for Trending	≥ 1 Dilution Lower # (%)	Exact #	≥ 1 Dilution Higher # (%)	Percent Difference (95% CI)	Statistically Significant Trending Noted
	Pseudomonas aeruginosa	39	21, (53.85)	18	0, (0)	-54%, (-68%, -36%)	Yes
Ceftriaxone	*Enterobacter cloacae* complex	12	3, (25)	4	5, (41.7)	17%, (-19%, 48%)	No
	Escherichia coli	16	5, (31.25)	2	9, (56.25)	25%, (-9%, 52%)	No
	Klebsiella aerogenes	15	7, (46.67)	5	3, (20)	-27%, (-53%, 7%)	No
	Klebsiella oxytoca	13	6, (46.15)	5	2, (15.38)	-31%, (-58%, 5%)	No
	Klebsiella pneumoniae group	15	4, (26.67)	1	10, (66.67)	40%, (4%, 64%)	Yes
	Proteus mirabilis	13	6, (46.15)	3	4, (30.77)	-15%, (-46%, 20%)	No
Cefuroxime	*Citrobacter koseri*	26	14, (53.85)	11	1, (3.85)	-50%, (-68%, -26%)	Yes
	Escherichia coli	225	131, (58.22)	83	11, (4.89)	-53%, (-60%, -46%)	Yes
	Klebsiella oxytoca	26	5, (19.23)	10	11, (42.31)	23%, (-2%, 45%)	No
	Klebsiella pneumoniae group	71	5, (7.04)	18	48, (67.61)	61%, (46%, 71%)	Yes
	Proteus mirabilis	17	11, (64.71)	3	3, (17.65)	-47%, (-68%, -14%)	Yes
Ciprofloxacin	*Citrobacter freundii* complex	11	0, (0)	3	8, (72.73)	73%, (34%, 90%)	Yes
	Enterobacter cloacae complex	12	1, (8.3)	5	6, (50)	42%, (5%, 67%)	Yes
	Escherichia coli	38	1, (2.63)	13	24, (63.16)	61%, (41%, 74%)	Yes
	Klebsiella aerogenes	18	1, (5.56)	11	6, (33.33)	28%, (1%, 51%)	No
	Klebsiella oxytoca	10	1, (10)	4	5, (50)	40%, (0%, 68%)	Yes
	Klebsiella pneumoniae group	17	3, (17.6)	3	11, (64.7)	47%, (14%, 68%)	Yes
	Proteus mirabilis	12	2, (16.67)	7	3, (25)	8%, (-24%, 39%)	No
	Proteus vulgaris	10	1, (10)	6	3, (30)	20%, (-16%, 51%)	No
	Serratia marcescens	20	0, (0)	9	11, (55)	55%, (29%, 74%)	Yes
	Pseudomonas aeruginosa	34	18, (52.94)	5	11, (32.35)	-21%, (-41%, 3%)	No
Ertapenem	*Escherichia coli*	15	10, (66.67)	2	3, (20)	-47%, (-69%, -11%)	Yes
	Klebsiella pneumoniae group	16	8, (50)	5	3, (18.75)	-31%, (-56%, 1%)	No
	Proteus mirabilis	9	3, (33.33)	4	2, (22.22)	-11%, (-46%, 28%)	No
	Proteus vulgaris	0	0,0	0	0,0	0	NA
Gentamicin	*Citrobacter freundii* complex	23	4, (17.39)	1	18, (78.26)	61%, (33%, 77%)	Yes
	Citrobacter koseri	15	5, (33.33)	3	7, (46.67)	13%, (-20%, 43%)	No

Drug	Organism Name	Total On Scale for Trending	≥ 1 Dilution Lower # (%)	Exact #	≥ 1 Dilution Higher # (%)	Percent Difference (95% CI)	Statistically Significant Trending Noted
	Escherichia coli	282	34, (12.06)	118	130, (46.1)	34%, (27%, 41%)	Yes
	Klebsiella aerogenes	33	1, (3.03)	8	24, (72.73)	70%, (49%, 82%)	Yes
	Klebsiella oxytoca	25	4, (16)	10	11, (44)	28%, (3%, 49%)	No
	Klebsiella pneumoniae group	75	4, (5.33)	14	57, (76)	71%, (57%, 80%)	Yes
	Proteus mirabilis	28	5, (17.86)	15	8, (28.57)	11%, (-11%, 32%)	No
	Proteus vulgaris	49	19, (38.78)	21	9, (18.37)	-20%, (-37%, -2%)	No
	Pseudomonas aeruginosa	42	10, (23.81)	25	7, (16.67)	-7%, (-24%, 10%)	No
	Serratia marcescens	26	2, (7.69)	9	15, (57.69)	50%, (25%, 68%)	Yes
Imipenem	*Acinetobacter baumannii* complex	15	12, (80)	3	0, (0)	-80%, (-93%, -48%)	Yes
	Citrobacter koseri	11	3, (27.27)	6	2, (18.18)	-9%, (-41%, 25%)	No
	Enterobacter cloacae complex	30	15, (50)	11	4, (13.33)	-37%, (-55%, -13%)	Yes
	Escherichia coli	29	4, (13.79)	7	18, (62.07)	48%, (24%, 66%)	Yes
	Klebsiella oxytoca	20	9, (45)	6	5, (25)	-20%, (-45%, 9%)	No
	Klebsiella pneumoniae group	47	9, (19.15)	7	31, (65.96)	47%, (27%, 62%)	Yes
	Pseudomonas aeruginosa	39	20, (51.28)	17	2, (5.13)	-46%, (-61%, -27%)	Yes
	Serratia marcescens	24	7, (29.17)	10	7, (29.17)	0%, (-25%, 25%)	No
Levofloxacin	*Citrobacter freundii*	16	6, (37.5)	9	1, (6.25)	-31%, (-56%, -2%)	Yes
	Citrobacter koseri	11	3, (27.27)	7	1, (9.09)	-18%, (-48%, 15%)	No
	Enterobacter cloacae complex	15	8, (53.3)	7	0, (0)	-53%, (-75%, -22%)	Yes
	Escherichia coli	86	12, (13.95)	57	17, (19.77)	6%, (-6%, 17%)	No
	Klebsiella aerogenes	18	13, (72.22)	5	0, (0)	-72%, (-88%, -43%)	Yes
	Klebsiella oxytoca	11	4, (36.36)	6	1, (9.09)	-27%, (-56%, 8%)	No
	Klebsiella pneumoniae group	29	17, (56.8)	11	1, (3.4)	-55%, (-71%, -33%)	Yes
	Proteus mirabilis	10	6, (60)	4	0, (0)	-60%, (-83%, -20%)	Yes
	Proteus vulgaris	13	2, (15.38)	9	2, (15.38)	0%, (-29%, 29%)	No
	Serratia marcescens	16	6, (37.5)	8	2, (12.5)	-25%, (-51%, 5%)	No
	Pseudomonas aeruginosa	43	4, (9.3)	21	18, (41.86)	33%, (14%, 48%)	Yes

Drug	Organism Name	Total On Scale for Trending	≥ 1 Dilution Lower # (%)	Exact #	≥ 1 Dilution Higher # (%)	Percent Difference (95% CI)	Statistically Significant Trending Noted
Meropenem	*A. baumannii-calcoaceticus* complex	28	20, (71.4)	8	0, (0)	-71%, (-85%, -49%)	Yes
	Enterobacter cloacae complex	24	9, (37.5)	6	9, (37.5)	0%, (-26%, 26%)	No
	Escherichia coli	14	8, (57.14)	1	5, (35.71)	-21%, (-50%, 14%)	No
	Klebsiella pneumoniae group	16	7, (43.75)	5	4, (25)	-19%, (-46%, 13%)	No
	Proteus mirabilis	34	5, (14.71)	10	19, (55.88)	41%, (19%, 59%)	Yes
	Proteus vulgaris	36	12, (33.33)	10	14, (38.89)	6%, (-16%, 26%)	No
	Serratia marcescens	13	9, (69.23)	1	3, (23.08)	-46%, (-70%, -8%)	Yes
	Pseudomonas aeruginosa	45	20, (44.44)	23	2, (4.44)	-40%, (-55%, -23%)	Yes
Meropenem/ Vaborbactam	*Citrobacter freundii* complex	15	7, (46.67)	6	2, (13.33)	-33%, (-58%, 0%)	Yes
	Citrobacter koseri	10	0, (0)	2	8, (80)	80%, (38%, 94%)	Yes
	Enterobacter cloacae complex	12	6, (50)	3	3, (25)	-25%, (-54%, 13%)	Yes
	Escherichia coli	15	4, (26.67)	4	7, (46.67)	20%, (-13%, 48%)	No
	Klebsiella aerogenes	10	7, (70)	2	1, (10)	-60%, (-81%, -17%)	Yes
	Klebsiella oxytoca	10	2, (20)	2	6, (60)	40%, (-2%, 67%)	No
	Klebsiella pneumoniae group	13	7, (53.85)	5	1, (7.69)	-46%, (-70%, -11%)	Yes
	Proteus mirabilis	21	2, (9.52)	6	13, (61.9)	52%, (24%, 71%)	Yes
Piperacillin/ Tazobactam	*Citrobacter koseri*	16	14, (87.5)	2	0, (0)	-88%, (-97%, -57%)	Yes
	Escherichia coli	72	46, (63.89)	14	12, (16.67)	-47%, (-59%, -32%)	Yes
	Klebsiella pneumoniae group	59	47, (79.7)	5	7, (11.9)	-68%, (-78%, -52%)	Yes
	Proteus vulgaris	1	0, (0)	0	1, (100)	100%, (-12%, 100%)	No
Tetracycline	*Acinetobacter baumannii* complex	12	4, (33.33)	6	2, (16.67)	-17%, (-47%, 18%)	No
	Escherichia coli	230	96, (41.74)	88	46, (20)	-22%, (-30%, -13%)	No
	Klebsiella aerogenes	36	20, (55.56)	9	7, (19.44)	-36%, (-54%, -14%)	Yes
	Klebsiella oxytoca	11	2, (18.18)	8	1, (9.09)	-9%, (-40%, 22%)	No
	Klebsiella pneumoniae group	69	32, (46.38)	24	13, (18.84)	-28%, (-41%, -12%)	No
Tobramycin	*Citrobacter freundii* complex	21	1, (4.76)	7	13, (61.9)	57%, (30%, 75%)	Yes

Drug	Organism Name	Total On Scale for Trending	≥ 1 Dilution Lower # (%)	Exact #	≥ 1 Dilution Higher # (%)	Percent Difference (95% CI)	Statistically Significant Trending Noted
	Citrobacter koseri	28	6, (21.43)	10	12, (42.86)	21%, (-3%, 43%)	No
	Enterobacter cloacae complex	32	0, (0)	6	26, (81.25)	81%, (62%, 91%)	Yes
	Escherichia coli	294	65, (22.11)	174	55, (18.71)	-3%, (-10%, 3%)	No
	Klebsiella aerogenes	46	8, (17.39)	33	5, (10.87)	-7%, (-21%, 8%)	No
	Klebsiella oxytoca	39	8, (20.51)	26	5, (12.82)	-8%, (-24%, 9%)	No
	Klebsiella pneumoniae group	105	14, (13.33)	59	32, (30.48)	17%, (6%, 28%)	No
	Proteus mirabilis	31	14, (45.16)	16	1, (3.23)	-42%, (-59%, -21%)	Yes
	Serratia marcescens	26	5, (19.23)	11	10, (38.46)	19%, (-5%, 41%)	No
	Pseudomonas aeruginosa	37	8, (21.62)	27	2, (5.41)	-16%, (-32%, 0%)	No
Trimethoprim /Sulfamethoxazole	*Escherichia coli*	30	4, (13.33)	0	26, (86.67)	73%, (50%, 85%)	Yes
	Klebsiella aerogenes	11	3, (27.27)	2	6, (54.55)	27%, (-12%, 57%)	No
	Klebsiella pneumoniae group	16	2, (12.5)	5	9, (56.25)	44%, (11%, 66%)	Yes

2. Matrix Comparison:

Blood Culture Bottle Compatibility/Equivalency

The VITEK REVEAL AST System was tested for compatibility with eleven different blood culture bottles from two manufacturers (Becton Dickinson BACTEC and bioMérieux BACT/ALERT). A panel of nine different bacterial isolates (one isolate each of *A. baumannii, E. cloacae*, *K. pneumoniae*, *K oxytoca*, *C. koseri*, and two isolates each of *E. coli*, and *P. aeruginosa*) were mixed with human whole blood, seeded directly into a blood culture bottle, and incubated for growth in a continuous monitoring blood culture system until indicated as positive for growth (i.e., bottle ring). Six replicates of each resulting positive blood culture were tested using the VITEK REVEAL GN AST kit at the time of positivity. Strict aerobic species (i.e., *Acinetobacter baumannii-calcoaceticus* complex members and *Pseudomonas aeruginosa*) were not tested in anaerobic bottles, based on the intended use of the bottles.

MIC results of each bottle type with each antimicrobial/organism combination were compared to the mode MIC value obtained with the broth microdilution reference method. Results for all the of antimicrobial/organism combinations for claimed species showed acceptable performance (≥ 89%) with all blood culture bottles.

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:

The FDA-recognized/approved susceptibility interpretive criteria for the antimicrobials evaluated with the VITEK REVEAL AST System are listed in **Table 12** below:

Table 12. FDA-Approved or Recognized Interpretive Criteria[1]

Antimicrobial	Organism	Minimum Inhibitory Concentration (µg/mL)		
		S	I	R
Amikacin	*Acinetobacter* spp. Enterobacterales *P. aeruginosa*	≤16	32	≥64
Amoxicillin/Clavulanate	Enterobacterales	≤8/4	16/8	≥32/16
Ampicillin/Sulbactam	Enterobacterales	≤8/4	16/8	≥32/16
Aztreonam	Enterobacterales	≤4	8	≥16
Cefepime	Enterobacterales	≤0.2	4-8*	≥16
	P. aeruginosa	≤8	-	≥16
Cefotaxime	*Acinetobacter* spp. Enterobacterales	≤1	2	≥4
Ceftazidime	*Acinetobacter* spp. Enterobacterales	≤8	4	≥16
	P. aeruginosa	≤8	-	≥16
Ceftazidime/Avibactam	Enterobacterales *P. aeruginosa*	≤8/4	-	≥16/4
Ceftolozane/Tazobactam	Enterobacterales	≤2/4	4/4	≥8/4
	P. aeruginosa	≤4/4	8/4	≥16/4
Ceftriaxone	Enterobacterales	≤1	2	≥4
Cefuroxime	Enterobacterales	≤8	-	≥16
Ciprofloxacin	Enterobacterales	≤0.25	0.5	≥1
	P. aeruginosa	≤0.5	1	≥2
Ertapenem	Enterobacterales	≤0.5	1	≥2
Gentamicin	Enterobacterales *P. aeruginosa*	≤4	8	≥16
Imipenem	*Acinetobacter* spp.	≤2	4	≥8

Antimicrobial	Organism	Minimum Inhibitory Concentration (µg/mL)		
		S	I	R
	Enterobacterales	≤1	2	≥4
	P. aeruginosa	≤2	4	≥8
Levofloxacin	Enterobacterales	≤0.5	1	≥2
	P. aeruginosa	≤1	2	≥4
Meropenem	Enterobacterales	≤1	2	≥4
	P. aeruginosa	≤2	4	≥8
Meropenem/Vaborbactam	Enterobacterales	≤4/8	8/8	≥16/8
Piperacillin/Tazobactam	Enterobacterales	≤8/4	16/4	≥32/4
Tetracycline	*Acinetobacter* spp. Enterobacterales	≤4	8	≥16
Tobramycin	Enterobacterales *P. aeruginosa*	≤4	8	≥16
Trimethoprim/Sulfamethoxazole	Enterobacterales	≤2/38	-	≥4/76

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

[1] FDA-Recognized Antimicrobial Susceptibility Test Interpretive Criteria Website https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm4 10971.htm

F Other Supportive Instrument Performance Characteristics Data:

Not applicable

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 breakpoint change protocol that was reviewed and accepted by FDA. 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 Specific Diagnostics intends to use to evaluate the VITEK REVEAL AST System when revised breakpoints for indicated antimicrobials are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, Specific Diagnostics will update the device 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.