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

I Background Information:

A 510(k) Number

K221688

B Applicant

Q-linea AB

C Proprietary and Established Names

ASTar Instrument and ASTar BC G- Kit

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

1. To obtain a substantial equivalence determination for use of the ASTar Instrument and ASTar BC G- Kit for testing positive blood culture samples to determine the minimum inhibitory concentration of specific antimicrobials with specific Gram-negative organisms.

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

B Measurand:

Antimicrobial	Reporting Range
Amikacin	≤0.5 to ≥256 µg/mL
Ampicillin	≤1 to ≥128 µg/mL
Ampicillin/sulbactam	≤1 to ≥128 µg/mL
Aztreonam	≤0.25 to ≥128 µg/mL
Cefazolin	≤0.25 to ≥32 µg/mL
Cefepime	≤0.25 to ≥128 µg/mL
Ceftazidime	≤0.25 to ≥128 µg/mL
Ceftazidime/avibactam	≤0.125 to ≥64 µg/mL
Cefuroxime	≤1 to ≥128 µg/mL
Ciprofloxacin	≤0.125 to ≥16 µg/mL
Gentamicin	≤0.25 to ≥64 µg/mL
Levofloxacin	≤0.125 to ≥32 µg/mL
Meropenem	≤0.06 to ≥128 µg/mL
Meropenem/vaborbactam	≤0.25 to ≥64 µg/mL
Piperacillin/tazobactam	≤0.25 to ≥512 µg/mL
Tigecycline	≤0.03 to ≥32 µg/mL
Tobramycin	≤0.06 to ≥64 µg/mL
Trimethoprim/sulfamethoxazole	≤0.06 to ≥16 µg/mL

C Type of Test:

Quantitative antimicrobial susceptibility test (AST) system that utilizes high-speed, time-lapse microscopy imaging of organisms in 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):

The ASTar System is intended to be used for the automated quantitative susceptibility testing for most clinically significant microorganisms. The ASTar System does not provide organism identification.

B Indication(s) for Use:

The ASTAar System, comprised of the ASTar Instrument with the ASTar BC G− Kit (ASTar BC G− Consumable kit, ASTar BC G− Frozen Insert, and ASTar BC G− Kit software), utilizes high-speed, time-lapse microscopy imaging of bacteria for the *in vitro*, quantitative determination of antimicrobial susceptibility of on-panel gram-negative bacteria. The test is performed directly on 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.

Test results from the ASTar BC G− Kit 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 ASTar BC G− panel, where inconclusive results are obtained, epidemiologic testing, recovery of organisms present in microbial samples, and susceptibility testing of bacteria in polymicrobial samples.

The ASTar BC G− Kit tests the following antimicrobial agents with the following bacterial species:

Amikacin: *Citrobacter freundii, Enterobacter cloacae* complex*, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Serratia marcescens*

Ampicillin: *Escherichia coli, Proteus mirabilis*

Ampicillin-sulbactam: *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris*

Aztreonam: *Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*

Cefazolin: *Klebsiella pneumoniae*

Cefepime: *Citrobacter freundii, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*

Ceftazidime: *Enterobacter cloacae* complex*, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*

Ceftazidime-avibactam*: Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Klebsiella oxytoca, Proteus mirabilis, Pseudomonas aeruginosa, Serratia marcescens*

Cefuroxime: *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis*

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

Gentamicin: *Citrobacter freundii, Citrobacter koseri, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*

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

Meropenem: *Acinetobacter baumannii, Citrobacter freundii, Citrobacter koseri, Escherichia coli, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*

Meropenem-vaborbactam: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Serratia marcescens*

Piperacillin-tazobactam: *Citrobacter koseri, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*

Tigecycline: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Serratia marcescens*

Tobramycin: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Serratia marcescens*

Trimethoprim-sulfamethoxazole: *Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus vulgaris*

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

General Limitations

- The ASTar BC G- kit can only be used with the ASTar Instrument.
- The ASTar BC G- kit has not been evaluated for specimens other than positive blood culture.
- The performance of the ASTar BC G- kit has only been evaluated using the following blood culture bottles:
    - bioMérieux BACT/ALERT FA Plus Aerobic
    - bioMérieux BACT/ALERT FN Plus Anaerobic
    - bioMérieux BACT/ALERT PF Plus Peds
    - bioMérieux BACT/ALERT SN Standard Anaerobic
    - bioMérieux BACT/ALERT SA Standard Aerobic
    - BD BACTEC Peds Plus
    - BD BACTEC Lytic Anaerobic
    - BD BACTEC Plus Anaerobic
    - BD BACTEC Plus Aerobic
    - BD BACTEC Standard Aerobic
    - BD BACTEC Standard Anaerobic
- The ASTar BC G− Kit should not be used with blood culture bottles containing charcoal.
- 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.
- Failure to observe proper procedures for sample collection, preparation, storage, handling and/or transportation may cause incorrect results.
- AST results should not be reported if two or more species are identified in a patient sample.
- If an AST result is not provided by the ASTar BC G- Kit, susceptibility testing must be performed using an alternate method.
- Subculturing of positive blood culture is necessary for organisms not claimed by the ASTar BC G- Kit and for antimicrobial agents not included on the ASTar panel.

Antimicrobial Susceptibility Testing (AST) Limitations

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

- The ability of the ASTar system to detect resistance in the following antimicrobial/organism combinations is unknown because of an insufficient number of resistant isolates were available during the clinical study:
  - Amikacin: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Serratia marcescens*
  - Ampicillin-sulbactam: *Citrobacter koseri, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris*
  - Aztreonam: *Citrobacter koseri, Klebsiella aerogenes, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*
  - Cefepime: *Citrobacter freundii, Citrobacter koseri, Klebsiella aerogenes, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*
  - Ceftazidime: *Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*
  - Ceftazidime-avibactam: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*
  - Cefuroxime: *Klebsiella oxytoca, Proteus mirabilis*
  - Ciprofloxacin: *Citrobacter koseri , Enterobacter cloacae* complex*, Klebsiella aerogenes, Klebsiella oxytoca, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*
  - Gentamicin: *Citrobacter freundii, Citrobacter koseri, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*
  - Levofloxacin: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* compex*, Klebsiella aerogenes, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*
  - Meropenem: *Citrobacter freundii, Citrobacter koseri, Escherichia coli, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*
  - Meropenem-vaborbactam: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris Serratia marcescens*
  - Piperacillin-tazobactam: *Citrobacter koseri, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*
  - Tigecycline: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Serratia marcescens*
  - Tobramycin: *Citrobacter freundii, Citrobacter koseri, Escherichia coli, Enterobacter cloacae complex, Proteus mirabilis, Serratia marcescens*
  - Trimethoprim-sulfamethoxazole: *Citrobacter koseri, Klebsiella aerogenes, Klebsiella oxytoca, Proteus vulgaris, Serratia marcescens*
- Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
  - Amikacin: *Acinetobacter baumannii, Escherichia coli, Proteus vulgaris*
  - Ampicillin-sulbactam: *Acinetobacter baumannii*

- Aztreonam: *Escherichia coli* when the ASTar MIC is 0.5 µg/mL due to one very major discrepancy, *Citrobacter freundii, Pseudomonas aeruginosa*
- Cefazolin: *Citrobacter koseri, Escherichia coli, Klebsiella oxytoca, Proteus mirabilis*
- Cefepime: *Proteus vulgaris* when the ASTar MIC is 32 µg/mL due to one major error, *Enterobacter cloacae complex*
- Cefotaxime: *Acinetobacter baumannii, Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*
- Ceftazidime: *Acinetobacter baumannii, Citrobacter freundii, Citrobacter koseri, Klebsiella aerogenes, Pseudomonas aeruginosa*
- Ceftazidime-avibactam: *Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae*
- Ceftolozane-tazobactam: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Serratia marcescens*
- Ceftriaxone: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Serratia marcescens*
- Cefuroxime: *Citrobacter koseri, Enterobacter cloacae complex, Klebsiella aerogenes*
- Ciprofloxacin: *Citrobacter freundii*
- Ertapenem: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*
- Gentamicin: *Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes*
- Meropenem: *Escherichia coli* when the ASTar MIC is either 0.5 or 1.0 µg/mL due to three very major discrepancies, *Enterobacter cloacae complex, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae*
- Piperacillin-tazobactam: *Escherichia coli* when the ASTar MIC is 8.0 µg/mL due to one very major discrepancy, *Klebsiella pneumoniae* when the ASTar MIC is 8.0 µg/mL due to two very major discrepancies; *Acinetobacter baumannii, Citrobacter freundii, Klebsiella aerogenes, Klebsiella oxytoca*
- Tobramycin: *Klebsiella pneumoniae* when the ASTar MIC is 4.0 µg/mL due to one very major discrepancy, *Klebsiella aerogenes, Klebsiella oxytoca, Proteus vulgaris, Pseudomonas aeruginosa*
- Trimethoprim-sulfamethoxazole: *Citrobacter freundii, Proteus mirabilis*

- Perform an alternate method of testing prior to reporting results when a resistant result is obtained for the following organisms, if critical to patient care:
  - Trimethoprim-sulfamethoxazole: *Klebsiella pneumoniae*

D Special Instrument Requirements:

Test with the following software or later version:

ASTar BC G- Kit Software version 1.6.4
ASTar Application Computer Image version 1.5
ASTar Instrument Computer Image version 1.7

IV Device/System Characteristics:

A Device Description:

ASTar System is a fully automated system for antimicrobial susceptibility testing (AST). It consists of the ASTar Instrument in combination with dedicated application kits. The ASTar BC G- Kit contains the ASTar BC G- Consumable kit (discs and cartridges), ASTar BC G- Frozen insert, and ASTar BC G- Kit software which must be installed on the instrument to process the kit. The frozen insert is a single-use plastic container with frozen reagents and is added to the cartridge prior to sample run. The system prepares an inoculum for AST and utilizes high-speed, time-lapse microscopy imaging of pathogens in broth microdilution to determine minimum inhibitory concentration (MIC) and qualitative susceptibility results for samples. Organism identification by an alternate method is required to be entered into the ASTar Instrument for AST results to be reported.

The ASTar instrument is designed to carry out sample preparation of up to six samples in parallel using a dedicated ASTar Cartridge consumable for each sample. In the subsequent AST culturing step, the instrument transfers the prepared sample into a second dedicated consumable, referred to as the ASTar Disc. Up to 12 discs can be incubated simultaneously in the system with samples at different stages of the processing procedure. New samples can be loaded in a random-access manner when there are available slots. The operator interacts with the instrument via the touchscreen display to run test samples.

ASTar BC G- Kit is used for *in vitro* determination of AST results for commonly isolated bacteria derived from positive blood culture samples confirmed by Gram stain to be Gram-negative bacteria. To start an analysis, approximately 1 mL of a positive blood culture is pipetted into the ASTar Cartridge by the operator and loaded into the system. The instrument purifies and quantifies the bacteria, and the bacterial concentration is adjusted to the appropriate inoculum concentration. The bacterial suspensions are transferred automatically to the ASTar Disc and antimicrobial susceptibility testing is performed based on a defined protocol. The system generates an MIC and further qualitative susceptibility results (i.e., S, I, R) for the tested antimicrobials, where applicable. The ASTar System with the ASTar BC G- Kit can determine the MIC of various antimicrobials when tested against specific organisms with FDA Susceptibility Testing Interpretive Criteria (STIC) breakpoints as shown in **Table 1** below.

Table 1: Reportable MIC Ranges and FDA Recognized Susceptibility Test Interpretive Criteria (STIC) / "Breakpoints" implemented in the kit software

Antimicrobial	ASTar System Reportable Range (µg/mL)	Enterobacterales			*P. aeruginosa*			*Acinetobacter* spp.		
		S	I	R	S	I	R	S	I	R
Ampicillin	≤1 to ≥128	≤8	16	≥32	-	-	-	-	-	-
Ampicillin-sulbactam	≤1 to ≥128	≤8	16	≥32	-	-	-	-	-	-
Ceftazidime-avibactam	≤0.125 to ≥ 64	≤8	-[a]	≥16	≤8	-[a]	≥16	-	-	-
Meropenem-vaborbactam	≤0.25 to ≥64	≤4	8	≥16	-	-	-	-	-	-
Piperacillin-tazobactam	≤0.25 to ≥512	≤8	16	≥32	-	-	-	-	-	-
Cefazolin	≤0.25 to ≥32	≤2	4	≥8	-	-	-	-	-	-

Antimicrobial	ASTar System Reportable Range (µg/mL)	Enterobacterales			*P. aeruginosa*			*Acinetobacter* spp.		
		S	I	R	S	I	R	S	I	R
Cefepime	≤0.25 to ≥128	≤2	4-8	≥16	≤8	-[a]	≥16	-	-	-
Cefuroxime	≤1 to ≥128	≤8	-[a]	≥16	-	-	-	-	-	-
Ceftazidime	≤0.25 to ≥128	≤4	8	≥16	≤8	-[a]	≥16	-	-	-
Aztreonam	≤0.25 to ≥128	≤4	8	≥16	-	-	-	-	-	-
Meropenem	≤0.06 to ≥128	≤1	2	≥4	≤2	4	≥8	≤2	4	≥8
Gentamicin	≤0.25 to ≥64	≤4	8	≥16	≤4	8	≥16	-	-	-
Tobramycin	≤0.06 to ≥64	≤4	8	≥16	-	-	-	-	-	-
Amikacin	≤0.5 to ≥256	≤16	32	≥64	≤16	32	≥64	-	-	-
Tigecycline	≤0.03 to ≥32	≤2	4	≥8	-	-	-	-	-	-
Ciprofloxacin	≤0.125 to ≥16	≤0.25	0.5	≥1	≤0.5	1	≥2	-	-	-
Levofloxacin	≤0.125 to ≥32	≤0.5	1	≥2	≤1	2	≥4	-	-	-
Trimethoprim-sulfamethoxazole	≤0.06 to ≥16	≤2	-[a]	≥4	-	-	-	-	-	-

[a]*No intermediate category is defined for these drug/organism combinations.*

B Principle of Operation:

The ASTar BC G- kit, along with the ASTar Instrument, constitute a fully automated system for the *in vitro* determination of antimicrobial susceptibility of Gram-negative bacilli present in positive blood culture bottles (BCBs). The instrument provides inoculum preparation for AST and utilizes high-speed, time-lapse microscopy imaging of pathogens in broth microdilution to determine minimum inhibitory concentration (MIC) and qualitative susceptibility results.

The consumable kit consists of a preparation cartridge and a disk with dried antimicrobials in 1:2 dilution series. Approximately 1 mL of a positive blood culture, confirmed Gram-negative by Gram stain, is pipetted into the ASTar Cartridge by the operator and loaded into the system. All other procedures are automated. Briefly, the ASTar purifies and quantifies the bacteria from the BCB. Resin particles are removed by filtration and human-derived cells are lysed by adding lysis buffer to the sample. Bacteria are separated from the lysate by filtering and captured on a filter membrane. The pathogens present in the aliquot are resuspended in culture medium. Bacterial concentration is determined by mixing an aliquot of bacterial suspension with staining medium (fluorescent dye). The stained aliquot is added to the disc and the concentration is determined by fluorescent imaging at one wavelength. Based on the concentration, the instrument creates aliquots at a pre-defined inoculum concentration (typically 5×10^5 CFU/mL). The disc is placed in an incubator carousel and each well is imaged at specified time intervals using a high-speed optical microscopy system. Bacterial growth and response to relevant concentrations of different antimicrobial drugs are measured throughout the incubation period using the optical detection system in combination with image analysis algorithms. Next, the images are analyzed for bacterial content over time, and the system generates the MIC and qualitative susceptibility results (i.e., S, I, R) for the tested antimicrobials, where applicable. The qualitative results are determined based on established breakpoints. The system allows culturing and analysis to start in the absence of bacterial ID, which is only needed for final interpretation and reporting. Results are available within approximately 6 hours.

C Instrument Description Information:

1. Instrument Name:
   ASTar Instrument

2. Specimen Identification:
   Barcodes link the cartridge and patient sample. Barcodes are located on the cartridge, disc, and frozen insert. These barcodes contain product information, lot information, and expiration date. A sample barcode is added by the operator to the cartridge on a dedicated area (only when running samples and not Quality Control strains). All barcodes on the cartridge and frozen insert are scanned when prompted. The disc barcode is scanned automatically by the instrument as the tray retracts. Materials not provided include a sterile device for safe transfer from positive blood culture (approximately 1 mL) and adhesive sample barcode label. Pathogen identification results from a separate method are entered into the ASTar Instrument to generate AST results.

3. Specimen Sampling and Handling:
   New samples can be loaded in a random-access manner if there are available slots for cartridges and discs. After placing the sample barcode in the dedicated area, approximately 1 mL of positive blood culture sample is added into the sample input of the cartridge. The end-user should check that the minimum fill-level is reached. Sample processing can be initiated without entering organism ID information, which is entered during or after processing of the sample to determine AST results.

4. Calibration:
   The ASTar System requires no calibration by the end-user. Adjustments and settings of mechanical optical components are carried out as part of the instrument production process and by field service engineers to address any issues with the instrument.

5. Quality Control:
   Quality control (QC) for AST testing of ASTar BC G− Consumable kit is performed by running pure cultures of characterized QC strains. An overnight culture of a QC strain is suspended in media (Cation-Adjusted Mueller-Hinton Broth, CAMHB) and added to the sample inlet of a cartridge (with a frozen insert added). For guidance, the bacterial suspension should be at 0.3–2.0 McFarland as measured in a densitometer. Cartridge and disc are loaded in the instrument and run. The instrument automatically determines the pathogen concentration, prepares the inoculum, and loads the inoculum into appropriate culture chambers in the disc. A QC test can be run at any time a slot in the instrument is available. Pass/fail status depends on whether the actual MIC result falls within the expected QC range (pass) or outside of the expected QC range (fail) (**Table 2**).

Table 2. QC Strains Tested with the ASTar System

Antimicrobial Agent	QC Strain	ASTar BC G− Reportable range[a] (µg/mL)	CLSI QC Organism range[a] (µg/mL)
Ampicillin	*E. coli* ATCC 25922 *K. pneumoniae* ATCC 700603[b]	≤0.5 - ≥128	2-8 >128[c]
Ampicillin-sulbactam	*E. coli* ATCC 25922 *K. pneumoniae* ATCC 700603	≤1 - ≥128	2–8 8–32
Ceftazidime-avibactam	*P. aeruginosa* ATCC 27853 *K. pneumoniae* ATCC 700603	≤0.06 - ≥64	0.5–4 0.25–2
Meropenem-vaborbactam	*P. aeruginosa* ATCC 27853 *K. pneumoniae* ATCC BAA 2814	≤0.06 - ≥64	0.125–1 0.125–0.5
Piperacillin-tazobactam	*P. aeruginosa* ATCC 27853 *K. pneumoniae* ATCC 700603	≤0.125 - ≥512 ≤0.25 - ≥512	1–8 8–32
Cefazolin	*E. coli* ATCC 25922	≤0.125 - ≥32	1–4
Cefepime	*P. aeruginosa* ATCC 27853	≤0.125 - ≥128	0.5–4
Cefuroxime	*E. coli* ATCC 25922	≤0.5 - ≥128	2–8
Ceftazidime	*P. aeruginosa* ATCC 27853 *K. pneumoniae* ATCC 700603[b]	≤0.125 - >128 ≤0.25 - ≥128	1–4 16–64
Aztreonam	*P. aeruginosa* ATCC 27853	≤0.125 - ≥128	2–8
Meropenem	*P. aeruginosa* ATCC 27853	≤0.03 - >128	0.125–1
Gentamicin	*P. aeruginosa* ATCC 27853	≤0.25 - ≥64	0.5–2
Tobramycin	*E. coli* ATCC 25922	≤0.06 - ≥64	0.25–1
Amikacin	*E. coli* ATCC 25922	≤0.125 - ≥256	0.5–4
Tigecycline	*E. coli* ATCC 25922	≤0.008 - ≥32	0.03–0.25
Ciprofloxacin	*P. aeruginosa* ATCC 27853	≤0.06 - ≥16	0.125–1
Levofloxacin	*P. aeruginosa* ATCC 27853	≤0.125 - ≥32	0.5–4
Trimethoprim-sulfamethoxazole	*E. coli* ATCC 25922	≤0.03 - ≥16	≤0.5

[a] *All concentrations are in µg/mL.*
[b] *Tested to confirm the integrity of the QC strain for testing with the beta-lactam/beta-lactam-inhibitor combination antimicrobial.*
[c] *ASTar MIC will report ≥128 µg/mL as an acceptable result.*

V Substantial Equivalence Information:

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

B Predicate 510(k) Number(s):
DEN160032

C Comparison with Predicate(s):

Device & Predicate Device(s):	**K221688 (Device)**	**DEN160032 (Predicate)**
Device Trade Name	ASTar BC G− Kit	Accelerate PhenoTest BC Kit
General Device Characteristic Similarities		
Intended Use/Indications For Use	The ASTar System is intended to be used for the automated quantitative susceptibility testing for most clinically significant microorganisms. The ASTar System does not provide organism identification. The ASTAar System, comprised of the ASTar Instrument with the ASTar BC G− Kit (ASTar BC G− Consumable kit, ASTar BC G− Frozen Insert, and ASTar BC G− Kit software), utilizes high-speed, time-lapse microscopy imaging of bacteria for the *in vitro*, quantitative determination of antimicrobial susceptibility of on-panel gram-negative bacteria. The test is performed directly on 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. Test results from the ASTar BC G− Kit 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 ASTar BC G− panel, where inconclusive results are obtained, epidemiologic testing, recovery of organisms present in microbial samples, and susceptibility testing of bacteria in polymicrobial samples.	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 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.
Blood Culture Bottle Types	BD BACTEC: Standard/10 Aerobic, Anaerobic; Lytic/10 Anaerobic; PEDS PLUS, Plus Aerobic, Anaerobic;	Same

Device & Predicate Device(s):	K221688 (Device)	DEN160032 (Predicate)
	BioMeriuex BacT/ALERT: Standard Aerobic, Anaerobic; Plus Aerobic, Anaerobic; PF Plus	
Technology	High-speed, time-lapse microscopy imaging	Similar
Sample Type	Positive Blood Culture	Same
Sample Prep	Automated direct from sample	Same
General Device Characteristic Differences		
IVD Function	Provides AST results only. ID is required but provided by alternative method	Provides both ID and AST
Instrument Platform	ASTar Instrument	Accelerate Pheno System
Blood Culture Bottle Type (Versa TREK:REDOX 1 and 2 Tested)	No	Yes
Antimicrobial Panel	Amikacin, Ampicillin, Ampicillin-sulbactam, Aztreonam Cefazolin, Cefepime, Ceftazidime, Ceftazidime-avibactam, Cefuroxime, Ciprofloxacin, Gentamicin, Meropenem, Meropenem-vaborbactam, Levofloxacin, Piperacillin-tazobactam, Tobramycin, Tigecycline, Trimethoprim-sulfamethoxazole	Amikacin, Ampicillin, Ampicillin-sulbactam, Aztreonam, Ceftazidime, Ceftaroline, Cefepime, Ceftriaxone, Ciprofloxacin, Daptomycin, Erythromycin, Ertapenem, Gentamicin, Linezolid, Meropenem, Piperacillin-tazobactam, Tobramycin, Vancomycin
Types Organisms Tested	Gram-negative bacteria	Gram-positive and Gram-negative bacteria
Sample per Instrument	12	1
Time to AST Results	Approximately 6 hours	Approximately 7 hours

VI Standards/Guidance Documents Referenced:

- IEC 60601-1-2 Edition 4.0 2014-02, Medical electrical equipment -Part 1-2: General requirements for basic safety and essential performance
- IEC 61010-1 Edition 3.1 2017-01, Safety requirements for electrical equipment for measurement, control, and laboratory use
- IEC 62304 Edition 1.1 2015-06 Consolidated Version, Medical device software - Software life cycle processes
- IEC 62366-1 Edition 1.1 2020-06 Consolidated Version, Medical devices - Part 1: Application of usability engineering to medical devices
- ISO 14971 Third Edition 2019-12 Medical devices - Application of risk management to medical devices
- ISO 15223-1 Fourth edition 2021-07 Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements
- ISO 20417 First edition 2021-04 Corrected version 2021-12 Medical devices- Information to be supplied by the manufacturer

- CLSI M100, 33rd Ed., 2021 Performance Standards for Antimicrobial Susceptibility Testing
- FDA Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA (Issued August 28, 2009)

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A reproducibility study for the ASTar System (ASTar BC G− Kit run on ASTar Instrument) with contrived positive blood culture bottles (BCBs) included the evaluation of 23 bacterial strains. Triplicate samples from each contrived blood culture were tested at three sites on at least two days. 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. All samples were tested within 16 hours of bottle positivity. Both best-case (assumes that off-scale results are within one dilution of the mode) and worst-case (assumes that off-scale results are more than one dilution of the mode) performance was determined for each antimicrobial. Antimicrobials with inter-site worst-case reproducibility of <89% or an insufficient number of results generated in the initial study were further evaluated in a supplemental study in which testing was performed with three instruments. The supplemental reproducibility study was conducted in-house with three individual instruments to increase the number of valid results. Testing was performed similar to the initial reproducibility study protocol.

Data from the Reproducibility Study are summarized in **Table 3** and show the performance for each drug with claimed species. In total, thirty-three (33) samples were re-run. Twenty (20) samples that did not complete a run were re-run under the same sample ID within 16 hours of positive BCB. Thirteen (13) samples were re-run with new inoculation with new sample ID due to ASTar instrument error, and 4 samples were withdrawn as these were duplicates. QC was run on the Q-linea ASTar system each day of reproducibility testing. Inter-site and intra-site reproducibility were determined to be acceptable.

Table 3. Reproducibility of ASTar System (ASTar BC G− Kit)

Antibiotic	Original reproducibility study results (3 sites)		Supplemental Study Data (single site)	
	Best-case[a]	Worst-case[b]	Best case[a]	Worst case[b]
Amikacin	144/144 (100%)	139/144 (96.5%)	53/53 (100%)	53/53 (100%)
Ampicillin[c]	118/126 (93.7%)	118/126 (93.7%)	36/36 (100%)	36/36 (100%)
Ampicillin-sulbactam	162/162 (100%)	162/162 (100%)	36/36 (100%)	34/36 (94.4%)
Aztreonam	108/108 (100%)	99/108 (91.7%)	18/18 (100%)[d]	18/18 (100%)[d]
Cefazolin	126/126 (100%)[e]	126/126 (100%)[e]	36/36 (100%)[e]	36/36 (100%)[e]
Cefepime	107/108 (99.1%)	107/108 (99.1%)	35/35 (100%)	35/35 (100%)
Ceftazidime	89/90 (98.9%)	82/90 (91.1%)	18/18 (100%)	13/18 (72.2%)
Ceftazidime-avibactam	89/89 (100%)	78/89 (88.8%)	18/18 (100%)	18/18 (100%)
Cefuroxime	125/125 (100%)	125/125 (100%)	36/36 (100%)	36/36 (100%)
Ciprofloxacin	144/144 (100%)	144/144 (100%)	53/53 (100%)	53/53 (100%)

Antibiotic	Original reproducibility study results (3 sites)		Supplemental Study Data (single site)	
	Best-case[a]	Worst-case[b]	Best case[a]	Worst case[b]
Gentamicin	108/108 (100%)	108/108 (100%)	53/53 (100%)	53/53 (100%)
Levofloxacin	180/180 (100%)	170/180 (94.4%)	71/71 (100%)	71/71 (100%)
Meropenem	36/36 (100%)[f]	36/36 (100%)[f]	36/36 (100%)	36/36 (100%)
Meropenem-vaborbactam	90/90 (100%)	90/90 (100%)	53/53 (100%)	53/53 (100%)
Piperacillin-tazobactam	233/233 (100%)	233/233 (100%)	53/53 (100%)	53/53 (100%)
Tigecycline	284/288 (98.6%)	284/288 (98.6%)	89/89 (100%)	89/89 (100%)
Tobramycin	263/270 (97.4%)	263/270 (97.4%)	87/89 (97.8%)	87/89 (97.8%)
Trimethoprim-sulfamethoxazole	180/180 (100%)	171/180 (95%)	0/0 (N/A)[g]	0/0 (N/A)[g]

[a]*Best case scenario calculation for reproducibility assuming the off-scale result is within one well from the mode.*
[b]*Worst case scenario calculation for reproducibility assuming the off-scale result is greater than one well from the mode.*
[c]*All antimicrobials show a reproducibility of ≥ 95% for best-case scenario calculations, except Ampicillin (93.7%). Supplemental testing with additional samples showed performance with ampicillin ≥95%.*
[d]*Aztreonam testing with other indicated species (not on panel) for drug: P. aeruginosa.*
[e]*Cefazolin testing with other indicated species (not on panel) for drug: E. coli and P. mirabilis.*
[f]*Meropenem reproducibility with all indicated species (not on panel) was 144/144 (100%) for best and worst case scenarios.*
[g]*No on-scale species tested for Trimethoprim-sulfamethoxazole.*

2. Linearity:

   Not Applicable

3. Analytical Specificity/Interference:
   Analytical Specificity—Not Applicable

   Interference Study
   The aim of this study was to demonstrate the ability of ASTar System to report accurate AST results in the presence of endogenous and exogenous substances in blood samples. Three (3) bacterial isolates from the following bacterial species were included in the analytical study: *E. coli, A. baumannii,* and *P. aeruginosa*. The isolates were selected to provide a variety of bacterial characteristics to demonstrate the robustness of the test and to include species that may be affected by the presence of the potential interferents. Organisms were inoculated into BCBs with and without interfering substances and cultured until positive. A purity check was performed on each positive BCB to verify that only monomicrobial samples were included in the study. Positive BCB (BD BACTEC Plus Aerobic/F Culture Vials Plastic) samples with and without the interferents were run on the ASTar System. All conditions were tested in triplicate. The MIC values obtained from the interferent samples were compared to the mode MIC results obtained from the samples without the potential interfering substances. If a MIC value was within ±1 doubling dilution from the initial value (without potential interferent), then the sample passed. At least one QC sample was run each day of testing on each instrument used that day. All QC isolates were run within each week on all instruments used that week. **Table 4** lists the potentially interfering endogenous and exogenous substances tested with the ASTar BC G- Kit.

Table 4. Potential Endogenous Interferents and Concentrations Tested for the ASTar BC G- Kit.

Potential Interferent	Concentration Tested
Endogenous Substances	
Conjugated bilirubin	400 mg/L
Gamma-globulin	50 g/L (plasma concentration)
RBCs (Hemoglobin/Hematocrit)	20 g/dL
WBC	12,000 WBCs/µL
Platelets	400,000 PLTs/µL
Exogenous Substances	
Intralipid	20 g/L
Sodium polyanethole sulfonate (SPS)[a]	0.1% w/v (in bottle with blood)
Heparin	3000 Units/L

[a]*Organisms were inoculated with SPS to match levels in BCBs. SPS in exogenous substances study tested at a higher concentration.*

All samples after spiking into blood turned positive as expected (within five days) and could be loaded onto the ASTar instruments as intended (within 16 hours of positivity). However, 10 samples failed during instrument run but could be re-run within 16 hours. In addition, six samples were re-run with new BCB inoculations because four samples failed an agar plate purity check, and two samples failed in the instrument but a re-run on the same day was not possible. One platelet interferent sample (*E. coli* QM324) gave no results after data re-analysis, due to a failed quality control of a positive growth control in the AST disc (indicating a defective consumable). This sample was not re-run since this information was available at the time of analysis, resulting in 112 samples included in the study. In total, 74 QC isolate samples were run. One (1) QC sample had to be re-run due to one failed MIC, which passed on the second run. In addition, five re-runs were required due to instrument related errors. Remaining QC samples yielded passed QC results for all antimicrobials.

All eight evaluated interfering substances had a >95% pass rate after comparison to samples without interferent (**Table 5).** No interference could be detected for any of the evaluated substances. The study results suggest that none of the tested interferents reduce quantitative AST performance of positive blood cultures run on the ASTar System.

Table 5. Performance with Potential Exogenous and Endogenous Interferents

Potential Interferent	Number of MIC values ±1 from mode MIC values of control sample/ Total number of evaluated MIC values	Pass rate
Conjugated bilirubin	117/117	100%
Gamma-globulin	117/117	100%
Intralipid	117/117	100%
SPS	117/117	100%
Heparin	117/117	100%
RBCs (Hemoglobin/Ht)	116/117	99.1%
WBCs	117/117	100%
Platelets	95/95	100%

Interfering Antibiotics Study

The aim of this study was to demonstrate if the presence of antibiotics in a positive blood culture sample can affect the ASTar System's capability to report AST results. Nine (9) bacterial isolates from the following bacterial species were included in the analytical study: *E. coli* (4), *K. pneumoniae* (4) and *P. aeruginosa* (1). Each potentially interfering antibiotic (i.e., Cefotaxime, Ciprofloxacin and Meropenem) was tested using three bacterial isolates from the nine (9) organism panel that were resistant to that antibiotic. In addition to the resistant isolates, a tenth (10^{th}) isolate (*K. pneumoniae*) that was sensitive to all three antibiotics was used in the study to confirm bioactivity of the antibiotic solutions. The MIC values obtained from the interferent samples were compared to the mode MIC values obtained from the control samples (no antibiotic) of the same isolate/BCB-combination. If the MIC value was within ±1 from the control value, then that MIC value passed. Results were pooled within each category (interfering antibiotic/BCB-combination) and the pass rate (%) when compared to control samples (without potential interferent) was determined. Mode MIC-values were determined for most control samples. However, in some cases the median MIC values were used as the control value instead.

Antibiotic test concentrations were selected to represent the highest expected drug concentration under therapeutic treatment (peak level) (**Table 6**). Positive BCB samples with and without the antibiotics were run on the ASTar System. Two different bottle types from two main suppliers were used—one containing resins (BD BACTEC Plus Aerobic/F Culture Vials Plastic) and the other lacking resins (bioMérieux BACT/ALERT SA Standard Aerobic). Each resistant isolate/antibiotic/BCB-combination was tested in triplicate. A purity check was performed on each positive BCB to verify that only monomicrobial samples were included in the study. The positive blood culture samples were then run on the ASTar System with kit consumables. At least one QC sample was run on each day of testing on every instrument used that day. All QC isolates were run within each week on all instruments used that week.

Table 6. Performance with Potentially Interfering Antibiotics

Antibiotic	Antibiotic class	Test concentration
Cefotaxime	Cephalosporin	52.8 mg/dL
Ciprofloxacin	Fluoroquinolone	1.20 mg/dL
Meropenem	Carbapenem	33.90 mg/dL

The study initially included 108 samples to be run on the ASTar System. All turned positive as expected (within five days) and could be loaded onto the study instruments as intended. Although10 samples failed during instrument run, these were re-run on the same day. In addition, two samples had to be re-run with new BCB inoculations because one sample failed an agar plate purity check and one sample failed in the instrument and a re-run on the same day was not possible. In total, 17 QC isolates were run. One re-run was required due to instrument related errors. The remaining QC isolates completed their ASTar runs, and all showed passed QC results for all antimicrobials.

Test results for each evaluated potentially interfering antibiotic are shown with pass rate (%) as compared to the control sample mode/median MIC values for the ASTar BC G- Kit (**Table 7**).

Table 7. Results of Potential Interferent (Antibiotic Study)

Interferent	BCB type[a]	Number of MIC values ±1 from mode value of control sample / Total number of evaluated MIC values	Pass Rate[b]
Cefotaxime	BACTEC	191/194	98.5%
	BACT/ALERT	192/192	100%
Ciprofloxacin	BACTEC	194/194	100%
	BACT/ALERT	189/195	96.9%
Meropenem	BACTEC	158/159	99.4%
	BACT/ALERT	152/158	96.2%

[a]BACTEC bottles contained resins whereas the BACT/ALERT bottles did not contain resins.

[b]Pass rates <90% was observed for some combinations of interferent/bottle type/antimicrobial. For these combinations the results are specified per antibiotic/bottle type (numbers within parenthesis show the ratio of passed replicates/total) as follows—Cefotaxime/BACTEC: Ceftolozane-tazobactam 88.9% (8/9), Trimethoprim-sulfamethoxazole 77.8% (7/9); Ciprofloxacin/BacT/ALERT: Amikacin 77.8% (7/9), Ampicillin-sulbactam 88.9% (8/9), Cefotaxime 88.9% (8/9), Tobramycin 77.8% (7/9); Meropenem / BACTEC: Trimethoprim-sulfamethoxazole 83.3% (5/6); Meropenem/BacT/ALERT: Meropenem-vaborbactam 50% (3/6), Trimethoprim-sulfamethoxazole 50% (3/6).

The combined total of potentially interfering antibiotics/BCB-combinations evaluated passed the acceptance criteria of >95% as compared to samples without interfering antibiotics.

4. Assay Reportable Range:

Not Applicable

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

Quality Control Testing. Quality control samples were run each day that testing was conducted. CLSI recommended 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 ASTar System, including the reference site using the broth microdilution reference method. QC organisms were tested on a rotating basis. QC expected ranges and results for the ASTar System are summarized in **Table 8**. For all antimicrobials, greater than 95% of results were within the expected range, which is acceptable.

Table 8. QC Expected Ranges and Results for the Quantitative ASTar System

Antimicrobial	QC Organism	Expected Range (µg/mL)	No. in Range (%)	
			ASTar	Reference
Ampicillin	*E. coli* ATCC 25922	2-8	149/149 (100)	108/108 (100)
	K. pneumoniae ATCC 700603[a]	>128[b]	144/144 (100)	117/117 (100)
Ampicillin/sulbactam	*E. coli* ATCC 25922	2-8	148/150 (98.7)	116/117 (99.1)
	K. pneumoniae ATCC 700603	8-32	146/146 (100)	114/116 (98.3)
Ceftazidime/avibactam	*P. aeruginosa* ATCC 27853	0.5-4	162/162 (100)	113/114 (99.1)
	K. pneumoniae ATCC 700603	0.25-2	146/146 (100)	115/115 (100)
Meropenem/vaborbactam	*P. aeruginosa* ATCC 27853	0.125-1	160/161 (99.4)	115/115 (100)
	K. pneumoniae ATCC BAA 2814	0.125-0.5	147/147 (100)	118/118 (100)
Piperacillin/tazobactam	*P. aeruginosa* ATCC 27853	1-8	162/162 (100)	115/116 (99.1)
	K. pneumoniae ATCC 700603	8-32	146/146 (100)	113/113 (100)
Cefazolin	*E. coli* ATCC 25922	1-4	150/150 (100)	116/117 (99.1)
Cefepime	*P. aeruginosa* ATCC 27853	0.5-4	161/162 (99.4)	118/119 (99.2)
Cefuroxime	*E. coli* ATCC 25922	2-8	150/150 (100)	115/116 (99.1)
Ceftazidime	*P. aeruginosa* ATCC 27853	1-4	161/161 (100)	109/110 (99.1)
	K. pneumoniae ATCC 700603[a]	16-64	146/146 (100)	115/115 (100)
Aztreonam	*P. aeruginosa* ATCC 27853	2-8	161/162 (99.4)	118/118 (100)
Meropenem	*P. aeruginosa* ATCC 27853	0.125-1	145/145 (100)	117/118 (99.2)
Gentamicin	*P. aeruginosa* ATCC 27853	0.5-2	159/159 (100)	116/116 (100)
Tobramycin	*E. coli* ATCC 25922	0.25-1	149/150 (99.3)	113/116 (97.4)
Amikacin	*E. coli* ATCC 25922	0.5-4	149/150 (99.3)	114/115 (99.1)
Tigecycline	*E. coli* ATCC 25922	0.03-0.25	149/150 (99.3)	114/115 (99.1)
Ciprofloxacin	*P. aeruginosa* ATCC 27853	0.125-1	160/162 (98.8)	111/112 (99.1)
Levofloxacin	*P. aeruginosa* ATCC 27853	0.5-4	162/162 (100)	114/115 (99.1)
Trimethoprim/ sulfamethoxazole	*E. coli* ATCC 25922	≤0.5	149/149 (100)	102/103 (99.0)

[a] *Tested to confirm the integrity of the QC strain for testing with the beta-lactam/beta-lactam-inhibitor combination antimicrobial.*

[b] *Highest concentration of Ampicillin on the ASTar BC G− panel is ≥128 µg/mL. ASTar MIC results of ≥128 µg/mL were considered acceptable.*

Microbial Suspension Accuracy Study

The objective of this study was to provide performance data supporting the ASTar System accuracy of bacterial concentration measurement and adjustment and to determine the system's capability to abort AST assay if a set low inoculum is detected. *E. coli, P. aeruginosa*, *E. cloacae complex* and *K. aerogenes* were included in this analytical study to represent a variety of species found in positive BCB, including two isolates that have been found to give high bacterial counts in positive BCBs. A dilution series (10-fold dilutions) consisting of six concentrations was prepared for each bacterial isolate. Each bacterial isolate

dilution was tested in triplicate for a total of 72 samples. Up to 12 samples were run per day on the ASTar System.

Seeded blood culture bottles using the four organisms were cultured until positive. Bottles seeded with blood in the absence of bacteria were also cultured in parallel. A viable count was performed on each positive BCB to determine the starting input concentration for the test system. Also, a purity check was performed on each positive BCB to verify that only monomicrobial samples were included in the study. Material from each positive BCB was then diluted in material from the BCBs without bacteria (negative) in five steps of ten-fold dilutions. A wide range of BCB input concentrations were prepared ($4.0 \times 10^3 – 4.3 \times 10^9$ CFU/mL). The undiluted sample and the dilution series were then loaded on the ASTar System with kit consumables. Samples were run in the ASTar System until the *"Eject"* function of the cartridge was available for each sample, i.e., when the AST wells were filled. The inoculum was extracted directly from cartridge and further diluted. Viable count for the bacterial input concentration of each sample (BCB viable count) and concentration-adjusted sample were reported. Viable count was performed on the concentration-adjusted sample within 15 minutes, except in cases where the instrument aborted the sample before the inoculum was prepared (i.e., when the bacterial count was already determined by the ASTar System to be out of range). Additionally, any samples which were automatically aborted by the instrument were recorded and the reason for run failure noted.

When run on the ASTar System, the concentration-adjusted samples of *E. coli, E. cloacae complex, P. aeruginosa* and *K. aerogenes* were required to be in a range of $2 – 8 \times 10^5$ CFU/mL by viable count in order to pass the acceptance criteria. A viable count was performed by plating three agar plates per sample and then calculating a mean CFU/mL. The viable count value was then used to assess the pass/fail criteria. The total pass rate was calculated using viable count data from all concentration-adjusted samples. If the mean CFU/mL was within acceptable range, the sample passed. On each study day where the ASTar System was run, at least one QC isolate was run on each operating instrument. In total, 11 QC isolates were run during the study. All QC samples yielded acceptable QC results.

Seventy-two (72) samples were included in the study (**Table 9**). Purity check was performed on all samples. Thirty-two (32) out of the 72 samples completed concentration adjustment by the ASTar System, and a subsequent viable count performed. Of these samples, the pass rate was 96.9% (31/32). Twenty-four (24) samples were within the ASTar System requirements input range of $5 \times 10^7 – 5 \times 10^9$ CFU/mL. 95.8% (23/24) of those samples completed the concentration adjustment step, and all these adjustments were within an acceptable range. Twelve (12) samples were in a concentration range between 5×10^6 and $< 4.99 \times 10^7$ CFU/mL. Of these, twelve samples, 75.0% (9/12) completed concentration adjustment with 88.9% (8/9) within an acceptable output range. Thirty-six (36) samples had a BCB concentration of $< 5 \times 10^6$ CFU/mL, where none of the samples completed the concentration adjustment step.

Table 9. BCB Viable Count Input Concentration Range and Distribution of Samples and Completed Concentration Adjustment by the ASTar System

BCB Input Viable Count (CFU/mL)	Quantity	Completed Concentration Adjustment	ASTar Output Viable Count within Acceptance Range
$\geq 5 \times 10^9$	0	0% (0/0)	N/A (0/0)
5×10^8 to $< 4.99 \times 10^9$	12	100% (12/12)	100% (12/12)
5×10^7 to $< 4.99 \times 10^8$	12	91.7% (11/12)	100% (11/11)
5×10^6 to $< 4.99 \times 10^7$	12	75.0% (9/12)	88.9% (8/9)[a]
$< 5 \times 10^6$	36	0% (0/36)	N/A (0/0)

[a]*The viable count for K. aerogenes QM409 sample was outside the acceptable range. This was likely due to an operator mistake, resulting in the wrong dilution plated for one of the three replicates used to determine viable count.*

Out of the 72 tested samples in this study, 40 samples did not complete the sample concentration adjustment step on the ASTar System and were aborted by the instrument. Of those 40 samples not completing sample concentration adjustment, 39/40 (97.5%) had BCB input concentrations determined to be below the ASTar System requirements of $5 \times 10^7 – 5 \times 10^9$ CFU/mL. Only one (1) sample (*P. aeruginosa* QM276) was within the system requirements and did not complete concentration adjustment. No samples in the study were above the 5×10^9 CFU/mL limit in system requirements. Samples that passed the concentration adjustment step had a BCB input concentration range between $2.4 \times 10^7 – 4.3 \times 10^9$ CFU/mL. The ASTar System was able to perform a concentration determination and adjustment for the majority of samples where the BCB input concentration was near the ASTar System requirements input range.

Sample Stability Study

The objective of this study was to provide data to support sample stability when samples come from blood culture bottles are stored either in blood culture cabinet or at room temperature. Nine (9) isolates from the following organisms were included in the study: *E. coli, K. oxytoca*, *K. pneumoniae, P. aeruginosa*, *P. mirabilis*, *E. cloacae, S. marcescens, C. koseri*, and *A. baumannii*. The isolates represent the product panel and were selected to favor resistance phenotypes and to include as many on-scale MIC values as possible. At least one QC sample was run each day of testing. The nine different isolates were run after three time/incubation conditions:

- <1 hour after positivity
- 16-24 hours RT after positivity
- 16-24 hours after positivity stored at 35 °C in the blood culture cabinet

The MIC values after 16-24 hours of incubation time (RT and 35 °C) were compared to the modal MIC values obtained from the samples run within one hour after positivity (**Table 10**). Mode MIC-values could be determined for most samples (<1 hour after positivity). In cases where a mode value could not be determined, the median was used. Results from all antimicrobials were pooled within each time/incubation condition. MIC values (within ±1 of the modal MIC value of samples loaded <1 hour) were evaluated for all time/incubation conditions. Overall, the number of MIC values of sample conditions tested within ±1 dilution to the mode value in the <1 hour sample were 100% (441/441) for 16-24 hours at RT and 99.6% (459/461) for 16-24 hours at 35 °C. Pass rates are shown below in **Table 10** at 16-18 hours and >18-24 hours at room temperature and at 35ºC.

Table 10. Pass Rate of Samples Loaded onto the ASTar System During Different Timeframes after BCB positivity[a]

Antimicrobial agent	Room Temperature		35 °C	
	16-18 hours[b,c]	>18-24 hours[b]	16-18 hours[b]	>18-24 hours[b]
Amikacin	1/1 (100%)	24/24 (100%)	3/3 (100%)	23/23 (100%)
Ampicillin	--	5/5 (100%)	3/3 (100%)	3/3 (100%)
Ampicillin-sulbactam	--	17/17 (100%)	3/3 (100%)	15/15 (100%)
Aztreonam	1/1 (100%)	21/21 (100%)	3/3 (100%)	20/20 (100%)
Cefazolin	--	14/14 (100%)	3/3 (100%)	12/12 (100%)
Cefepime	1/1 (100%)	21/21 (100%)	3/3 (100%)	20/20 (100%)
Ceftazidime	1/1 (100%)	24/24 (100%)	3/3 (100%)	23/23 (100%)
Ceftazidime-avibactam	1/1 (100%)	21/21 (100%)	3/3 (100%)	20/20 (100%)
Cefuroxime	--	17/17 (100%)	3/3 (100%)	14/14 (100%)
Ciprofloxacin	1/1 (100%)	21/21 (100%)	3/3 (100%)	20/20 (100%)
Gentamicin	1/1 (100%)	21/21 (100%)	3/3 (100%)	20/20 (100%)
Levofloxacin	1/1 (100%)	21/21 (100%)	3/3 (100%)	20/20 (100%)
Meropenem	1/1 (100%)	24/24 (100%)	3/3 (100%)	23/23 (100%)
Meropenem-vaborbactam	--	19/19 (100%)	3/3 (100%)	17/17 (100%)
Piperacillin-tazobactam	--	22/22 (100%)	3/3 (100%)	19/20 (95.0%)
Tigecycline	--	17/17 (100%)	--	16/17 (94.2%)
Tobramycin	1/1 (100%)	21/21 (100%)	3/3 (100%)	20/20 (100%)
Trimethoprim-sulfamethoxazole	--	19/19 (100%)	3/3 (100%)	17/17 (100%)
Total	11/11 (100%)	430/430 (100%)	63/63 (100%)	396/398 (99.5%)

[a] Bottle type was the BD BACTEC Plus Aerobic medium in plastic culture vials.
[b]Stability of samples loaded to the ASTar System within different timeframes after BCB positivity for each time/incubation condition. The pass rate represents the number of MIC values ±1 from mode MIC values in initial sample (<1 hour)/total MIC values at that condition. Data also includes indicated species, but not claimed, due to panel alteration after the study was completed.
[c]Greater number of data points collected across the panel of antimicrobials under more challenging conditions related to time (>18 hrs) and temperature (35ºC).

In total, 103 positive blood culture samples were loaded onto the ASTar System. Eight (8) samples failed during instrument run and did not generate MIC results; however, these were re-run within the respective timeframe using the same positive BCB. Twelve (12) samples had to be re-run with a new BCB inoculation due to failed purity check. Two (2) samples were accidentally taken out of cabinet before turning positive and had to be re-run with new BCB inoculations. Two samples (*E. cloacae*, 16-24 hours at 35 °C, and *P. mirabilis*, 16-24 hours at RT) gave no results due to a failed quality check of a positive growth control in the ASTar disc (indicating a defect consumable). One (1) additional sample (*S. marcescens*, 16-24 hours at RT) yielded no results due to a delay in transfer of ASTar culture images during the run. These last three samples were not re-run at the time of sample testing. In total 64 QC isolate samples were run during the study. Two (2) QC samples failed QC results in the initial run (*E. coli* ATCC 25922 run with Cefazolin), but were successfully re-run. Three (3) QC samples were re-run successfully after instrument related errors, and one (1) QC sample was not re-run within the week it failed. Remaining QC samples yielded acceptable results for all antimicrobials.

Samples stored for up to 16 hours after positivity at either room temperature or in 35 °C in a blood culture cabinet produced similar results to samples loaded into the ASTar instrument within 1-hour of positivity. Language will be added to labeling to indicate positive blood cultures should be *"tested immediately after a positive flag,"* as well as language indicating that testing within 16 hours of positivity may be performed in case of instrument errors or if re-testing is needed.

6. Detection Limit:
   Not Applicable

7. Assay Cut-Off:

   Not Applicable

8. Accuracy (Instrument):

   Not Applicable

9. Carry-Over:
   The objective was to provide supporting data of the ASTar Systems' ability to run multiple samples in parallel without carry-over or cross contamination between samples. Two (2) isolates of *E. coli*—one highly resistant and one susceptible —were included in this analytical study. MIC values for the two *E. coli* isolates differed for several antimicrobials. BCBs (BD BACTEC Plus Aerobic/F Culture Vials Plastic) were seeded separately with each isolate and spiked into healthy human donor blood and incubated until positive. Positive BCB samples were then run on the ASTar System within 16 hours of positive BCB ring. Up to 12 samples were run per day on the ASTar System. The operators loaded and started a run of 6 samples with either alternating susceptible or resistant isolates or a full run of the isolate in each ASTar instrument. At least one QC sample was run each day of testing on every ASTar Instrument used that day. The MIC values of isolates tested in parallel were within ± 1 dilution compared to the mode MIC values for each respective strain. When evaluating the susceptible isolate samples, no carry-over or cross contamination was observed as evidenced by 99.7% total pass rate (307/308). In conclusion, the ASTar System was capable of running multiple samples in parallel without carry-over or cross contamination between samples.

   For re-runs, two (2) samples required re-runs due to sample failures and were re-loaded within 16 hours. Six (6) samples required re-runs on another day with new BCB inoculations due to a single system failure. During re-run, a full alternated isolate run with six samples was loaded to ASTar, which resulted in three additional datapoints for a total of 27 samples. In total, 11 QC isolate samples were run on ASTar instruments during the study. Two (2) out of 11 QC samples were additional re-runs due to sample and system failures on ASTar; all antimicrobials had a passed QC result on each instrument.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   The purpose of the clinical study was to demonstrate the clinical performance of the ASTar BC G- Kit with the ASTar Instrument in providing quantitative AST results direct from

positive blood culture containing Gram-negative bacteria. Results were compared to reference frozen Broth Microdilution (BMD) results performed according to CLSI M07. Positive blood cultures included fresh, left-over samples from patients with suspected bacteremia, along with positive blood cultures contrived with clinical stock isolates from the clinical sites or challenge isolates. Clinical stock isolates and challenge isolates were enrolled to supplement fresh positive blood cultures due to low prevalence of certain species and antimicrobial resistance expected during prospective collection. Isolates were sub-cultured on appropriate media (Tryptic Soy Agar with 5% sheep blood), spiked into blood culture bottles at a concentration of 10^3 to 10^4 CFU per bottle containing fresh human donor blood, and incubated on the appropriate blood culture system until ring positivity.

Clinical performance testing on the ASTar System was initially performed at four sites (3 U.S. test sites and 1 internal site). For instances in which testing was required to supplement existing data from the original study and support specific claims, testing was performed on ASTar System instruments at three testing sites (2 US and one internal). Testing with the ASTar BC G− Kit on the ASTar Instrument was performed within 16 hours of blood culture positivity during which time the blood culture bottle was either kept on the automated blood culture instrument or stored at room temperature until testing. Organism identification was obtained from an FDA cleared bacterial identification method and/or FDA cleared MALDI-TOF method for input into the ASTar Instrument. An aliquot from contrived positive blood cultures was sub-cultured onto Tryptic Soy Agar with 5% Sheep Blood or other appropriate media plate and incubated for 18-24 hours. Isolation plates were checked for purity and colony morphology, which was used to verify isolate identification via MALDI. If more than one colony type was observed, each colony type was isolated for purity assessment. If direct-from-blood culture ID system (first bacterial ID method) results were not available or if the results from the specified ID method did not provide a specific species on the ASTar panel, results from MALDI were performed on subcultured isolates and used for input into the ASTar System. During the study, MALDI was performed on all isolates for confirmation. MALDI from the subcultured organism was used for final organism identification. If more than one organism was identified by the first bacterial ID method, the ASTar test was aborted or the pathogen ID not entered in the ASTar Instrument, and the sample was excluded from the final performance data according to the exclusion criteria. Samples with multiple organisms were tracked and reported as mixed or polymicrobial.

A total of 1,068 samples were enrolled in the study that included both Fresh PBC (positive blood cultures) and contrived PBC with either clinical stock or challenge isolates. 188 samples were excluded due to off-panel organisms, contamination of contrived samples (either due to the blood used for contriving or other sources), non-viable stock isolates, and protocol deviations. In total 880 samples were included in the performance analysis consisting of 256 fresh, positive blood culture samples (29.1%), 223 contrived samples with clinical stock isolates (25.3%), and 401 contrived blood culture samples with challenge isolates (45.6%). In the choice of clinical stock isolates, on-panel organisms (i.e., Gram-negative bacteria species included in the ASTar BC G- panel) were selected from isolate banks at the external clinical sites to supplement species and antimicrobial resistance requirements. These isolates were originally sourced from clinical specimens from patients admitted at the clinical site. Pure isolates were cultured and contrived in blood cultures using healthy human donor blood and enrolled and tested after positivity. The set of challenge isolates were provided for testing at both the internal clinical site and selected external clinical sites. These challenge isolates included CDC AR Bank isolates obtained in the

United States as well as isolates obtained from clinical samples at hospitals throughout Europe. Challenge isolates were used to supplement Fresh PBC and contrived stock isolates for species inclusion, specific antimicrobial resistance, and on-scale MIC results closer to the breakpoints. In addition, challenge isolates were shipped to the central reference site for BMD testing and characterization. Subsequently, selected on-panel challenge isolates were cultured and contrived in blood cultures using healthy human donor blood, and enrolled and tested after ring positivity. ASTar BC G- Kit testing was compared to frozen BMD run in triplicate according to CLSI to establish a reference Mode MIC for each antimicrobial evaluated. If a Mode MIC could not be established with the first set of three replicates a second set of three frozen replicates was tested. If a Mode MIC could not be established with the second set of plates, the Median from all six plates was used. A total of 933 valid samples were analyzed on the ASTar during the clinical study and 97.2% (907/933) of samples produced at least a partial AST result. Of the 26 samples that failed to produce an AST result, 96% (25/26) were resolved upon retesting.

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 ASTar MIC results that were within plus or minus one serial two-fold dilution of the reference result. CA was calculated as the percentage of ASTar interpretive results (S/I/R) that were identical to the interpretive results of the reference result. EA of evaluable results (on-scale ASTar 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 criterion, 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 ASTar BC G- Kit AST System performance is described below for each antimicrobial and indicated species. Complete details and results including EA, CA and error rate analyses are summarized in **Table 11**.

Ampicillin. A total of 236 Enterobacterales isolates (202 *E. coli*, 34 *P. mirabilis*) were evaluated with ampicillin. The combined results from clinical and challenge testing demonstrated an EA of 97.5% and CA of 97.9%. There were 3 minor, 2 major, and 0 very major errors. Overall, performance was acceptable.

Amikacin. A total of 49 *A. baumannii* isolates were evaluated with amikacin. The combined results from clinical and challenge testing demonstrated an EA of 89.8% and CA of 85.7%, which was not acceptable. There were 6 minor,1 major (1/36 = 2.8%), and 0 very major errors. Due to the unacceptable performance for *A. baumannii*, this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *A. baumannii* due to unacceptable performance:

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

- Amikacin: *Acinetobacter baumannii*

A total of 64 *P. aeruginosa* isolates were evaluated with amikacin. The combined results from clinical and challenge testing demonstrated an EA of 92.2% and CA of 96.9%. There were 2 minor, 0 major, and 0 very major errors. Overall, performance was acceptable.

A limitation statement is included in the device labeling to address the lack of testing with resistant *Pseudomonas aeruginosa* isolates.

A total of 735 Enterobacterales isolates (indicated species: 200 *E. coli*, 65 *E. cloacae* complex, 27 *C. freundii*, 48 *K. aerogenes*, 50 *K. oxytoca*, 142 *K. pneumoniae*, 89 *P. mirabilis*, 33 *P. vulgaris*, 39 *S. marcescens*; non-indicated species: 42 *C. koseri*) were evaluated with amikacin. The combined results from clinical and challenge testing demonstrated an EA of 86.7% and CA of 99.1%. There were 7 minor, 0 major, and 0 very major errors. When evaluating results by individual species, *E. coli* had an EA of 68% and CA of 99% with 2 minor, 0 major, and 0 very major errors. The performance was not acceptable. *P. vulgaris* had an EA of 81.8% with 0 minor, 0 major, and 0 very major errors. The performance was not acceptable. Due to the unacceptable performance for *E. coli* and *P. vulgaris*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *E. coli* and *P. vulgaris* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Amikacin: *Escherichia coli*, *Proteus vulgaris*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter koseri*, *Citrobacter freundii, Enterobacter cloacae* complex*, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis,* and *Serratia marcescens* isolates.

Ampicillin-Sulbactam. A total of 49 *A. baumannii* isolates were evaluated with ampicillin-sulbactam. The combined results from clinical and challenge testing demonstrated an EA of 89.8% and CA of 71.4%. The EA of evaluable for *A. baumannii* was 88.6%, which was not acceptable. In addition, there were 13 minor, 1 major (1/28=3.6%), and 0 very major errors, which was not acceptable. Due to the unacceptable performance for *A. baumannii,* this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *A. baumannii* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Ampicillin-Sulbactam: *Acinetobacter baumannii*

A total of 487 Enterobacterales isolates (indicated species: 201 *E. coli*, 50 *K. oxytoca*, 140 *K. pneumoniae*, 34 *P. mirabilis,* 20 *P. vulgaris*; non-indicated species: 42 *C. koseri*) were evaluated with ampicillin-sulbactam. The combined results from clinical and challenge testing demonstrated an EA of 97.3% and CA of 90.1%. There were 47 minor, 1 major, and 0

very major errors. When evaluating results by individual species, *K. oxytoca* had a CA <90%, which was considered acceptable since all of the categorical errors were minor and the EA of evaluable results was good (>95%). *P. vulgaris* had an EA of 85% and CA of 95%. The EA of the evaluable was 85%, which was low. However, analysis of performance of *P. vulgaris* using a truncated reporting range (≤2 µg/mL - ≥128 µg/mL) improved the EA to 90%. This performance was acceptable.

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter koseri, Klebsiella oxytoca*, *Proteus mirabilis,* and *Proteus vulgaris* isolates.

Aztreonam. A total of 679 Enterobacterales isolates (201 *E. coli,* 42 *C. freundii,* 42 *C. koseri,* 65 *E. cloacae* complex*,* 48 *K. aerogenes,* 49 *K. oxytoca,*141 *K. pneumoniae,* 34 *P. mirabilis,* 18 *P. vulgaris,* 39 *S. marcescens*) were evaluated with aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 96.2% and CA of 96.3%. There were 20 minor, 0 major, and 5 very major errors. When evaluating results by individual species, *C. freundii* had a CA <88.1% and EA of Evaluable of <69.2% with 4 minor, 0 major, and 1 (1/13=7.7%) very major errors. The performance was unacceptable. For *K. oxytoca*, an EA of 85.7% was observed with a CA of 98% with 0 minor and 0 major errors. One 1(1/4=25%) very major error was observed, which was considered a random error due to the limited number of resistant isolates tested. Analysis of performance of *K. oxytoca* using a truncated reporting range (≤0.25 µg/mL- ≥128 µg/mL) improved the EA to 93.9%. This performance was acceptable. *E. coli* showed 2 very major errors (2/52=3.8%)—one of which was at ASTar MIC value of 0.5 µg/mL (representing 8.2%) of results from this drug/organism combination. Restricting the reporting at an MIC value of 0.5 µg/mL mitigated one very major error and was acceptable. For *P. vulgaris*, 1 very major error was reported, which was considered a random error due to the limited number of resistant isolates tested. Due to the unacceptable performance for *C. freundii,* this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to address one of the *E. coli* very major errors and restrict reporting of *C. freundii* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Aztreonam: *Escherichia coli* when the ASTar MIC is 0.5 µg/mL due to 1 very major error; *Citrobacter freundii*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter koseri, Klebsiella aerogenes, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris*, and *Serratia marcescens* isolates.

A total of 64 *P. aeruginosa* isolates were evaluated with aztreonam. The combined results from clinical and challenge testing demonstrated an EA of 87.5% and CA of 76.6%. There were 11 minor, 0 major, and 4 very major (4/22 = 18.2%) errors. Due to the unacceptable performance for *P. aeruginosa*, this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *P. aeruginosa* due to unacceptable performance:

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

- Aztreonam: *Pseudomonas aeruginosa*

Cefazolin. A total of 351 Enterobacterales isolates (indicated species: 49 *E. coli*, 50 *K. oxytoca*, 140 *K. pneumoniae*, 90 *P. mirabilis*; non-indicated species: 22 *C. koseri*) were evaluated with cefazolin. The combined results from clinical and challenge testing demonstrated an EA of 89.2% and CA of 76.1%. There were 72 minor, 11 major, and 1 very major errors. When evaluating results by individual species, *C. koseri* had an EA of 63.6% and CA of 45.4%, which was unacceptable. *E. coli* had an EA of 85.7% and CA of 81.6% with 4 minor, 5 (5/26=19.2%) major, and 0 very major errors, which was not acceptable. *K. oxytoca* had an EA of 80% and CA of 72% with 12 minor, 2 major (2/10=20%), and 0 very major errors, which was not acceptable. For *K. pneumoniae*, the CA was <90%, which was considered acceptable since most of the categorical errors were minor and the EA of evaluable results was good (93.5%). *P. mirabilis* had an EA of 91.1% and CA of 64.4% with 30 minor, 2 major (2/4=100%), and 0 very major errors with an EA of evaluable of 90.6%. However, the 2 (2/4=50%) major errors yielded an unacceptable major error rate. Due to the unacceptable performance for *C. koseri, E. coli, K. oxytoca,* and *P. mirabilis*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting of C. *koseri, E. coli, K. oxytoca*, and *P. mirabilis* due to unacceptable performance:

Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:

- Cefazolin: *Citrobacter koseri*, *Escherichia coli, Klebsiella oxytoca*, *Proteus mirabilis*

Cefepime. A total of 738 Enterobacterales isolates (indicated species: 41*C. freundii*, 64 *E. cloacae* complex, 202 *E. coli*, 49 *K. aerogenes*, 50 *K. oxytoca,* 141 *K. pneumoniae,* 90 *P. mirabilis,* 20 *P. vulgaris,* 39 *S. marcescens;* non-indicated: 42 *C. koseri*) were evaluated with cefepime. The combined results from clinical and challenge testing demonstrated an EA of 95.1% and CA of 95.5%. There were 31 minor, 2 major, and 0 very major errors. When evaluating results by individual species, *E. cloacae* complex had an EA of 92.2% and CA of 85.9% with 9 minor, 0 major, and 0 very major errors. This was not acceptable as the EA of the evaluable was only 79.2%. Due to the unacceptable performance for *E. cloacae* complex, this drug/organism combination is not indicated for use with the ASTar System. *P. vulgaris* had 1 major error at MIC value of 32 µg/mL, which represented 5.3% (1/19) major error rate with this drug/organism combination. The following limitation statement is included in device labeling to address the *P. vulgaris* major error and restrict reporting of *E. cloacae* complex due to unacceptable performance:

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

- Cefepime: *Proteus vulgaris* when the ASTar MIC is 32 µg/mL due to one major error; *Enterobacter cloacae* complex

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter, freundii, Citrobacter koseri, Klebsiella aerogene, Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris, and Serratia marcescens* isolates.

A total of 64 *P. aeruginosa* isolates were evaluated with cefepime. The combined results from clinical and challenge testing demonstrated an EA of 93.8% and CA of 89.1%. There were 3 major (3/42 = 7.1%) and 4 very major (4/22 = 18.2%) errors. Three of the 3 major errors and 4 of the 4 very major errors had an MIC value that was in essential agreement with the reference MIC value. Therefore, the adjusted major error rate (0/42) and very major error rates (0/22) were 0%, which was acceptable.

Cefotaxime. A total of 49 *A. baumannii* isolates were evaluated with cefotaxime. The combined results from clinical and challenge testing demonstrated an EA of 85.7% and CA of 95.9%. There were 2 minor, 0 major, and 0 very major errors. Overall, performance was not acceptable. Due to the unacceptable performance for *A. baumannii,* this drug/organism combination is not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting of *A. baumannii* due to the unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:
> - Cefotaxime: *Acinetobacter baumannii*

A total of 735 Enterobacterales isolates (43 *C. freundii,* 41*C. koseri,* 65 *E. cloacae* complex, 202 *E. coli*, 49 *K. aerogenes*, 49 *K. oxytoca*, 140 *K. pneumoniae*, 90 *P. mirabilis,* 34 *P. vulgaris,* 22 *S. marcescens*) were evaluated with cefotaxime. The combined results from clinical and challenge testing demonstrated an EA of 82.7% and CA of 97.7%. There were 6 minor, 1 major, and 10 very major errors. When evaluating results by individual species, *C. freundii* had an EA of 76.7% and CA of 95.4% with 1 minor, 0 major, and 1 (1/14=7.1%) very major errors, which was not acceptable. *C. koseri* had an EA of 87.8% and CA of 100% with 0 minor, 0 major, and 0 very major errors. The EA of evaluable was 87.8%. This performance was unacceptable. *E. coli* had an EA of 89.6% and CA of 97.5% with 0 minor, 1 major (1/138=0.7%), and 4 (4/64=6.3%) very major errors, which was unacceptable. *K. aerogenes* had an EA of 77.6% and CA of 95.2% with 1 minor, 0 major, and 1 (1/11=9%) very major errors, which was unacceptable. *K. oxytoca* had an EA of 69.4% and CA of 93.9% with 1 minor, 0 major, and 2 (2/4=50%) very major errors, which was unacceptable. *P. vulgaris* had an EA of 58.8% and CA of 94.1% with 1 minor, 0 major, and 1(1/1=100%) very major errors, which was not acceptable. *K. pneumoniae* had an EA of 88.6% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was not acceptable. *P. mirabilis* had an EA of 73.3% and CA of 98.9% with 1 minor, 0 major, and 0 very major errors, which was unacceptable. *S. marcescens* had an EA of 72.7% and CA of 95.5% with 0 minor, 0 major, and 1 very major errors (1/1=100%), which was unacceptable. Due to the unacceptable performance for *C. freundii, C. koseri, E. coli, K. aerogenes, K. oxytoca, K. pneumoniae, P. mirabilis, P. vulgaris*, and *S. marcescens*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting for *C. freundii, C. koseri, E. coli, K. aerogenes, K. oxytoca, K. pneumoniae, P. mirabilis, P. vulgaris, and S. marcescens* due to unacceptable performance:

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

- Cefotaxime: *Citrobacter freundii*, *Citrobacter koseri*, *Escherichia coli*, *Enterobacter cloacae complex, Klebsiella aerogenes, Klebsiella oxytoca*, *Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris,* and *Serratia marcescens.*

Ceftazidime. A total of 48 *A. baumannii* isolates were evaluated with ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 91.7% and CA of 87.5%. There were 6 minor, 0 major, and 0 very major errors. In addition, the EA of evaluable results was 86.2% (25/29). Due to the unacceptable performance for *A. baumannii*, this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *A. baumannii* due to unacceptable performance:

Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
- Ceftazidime: *Acinetobacter baumannii*

A total of 682 Enterobacterales isolates (43 *C. freundii,* 42 *C. koseri,* 64 *E. cloacae,* 202 *E. coli*, 48 *K. aerogenes,* 49 *K. oxytoca,* 141 *K. pneumoniae*, 34 *P. mirabilis,* 20 *P. vulgaris,* 39 *S. marcescens*) were evaluated with ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 87.2% and CA of 96.6%. There were 16 minor, 4 major, and 3 very major errors. When evaluating results by individual species, *C. freundii* had an EA of 83.7% and CA of 95.4% with 1 minor, 0 major, and 1(1/13=7.6%) very major errors, which was not acceptable. *C. koseri* had an EA of 83.3% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was not acceptable. *E. coli* had an EA of 86.6% and CA of 94.1% with 10 minor, 1 major (1/144=0.7%), and 1 (1/50=2%) very major errors. Analysis of performance of *E. coli* using a truncated reporting range ($\leq$0.25 µg/mL - $\geq$128 µg/mL) improved the EA to 97.5%, which was acceptable. *K. aerogenes* had an EA of 68.8% and CA of 93.8% with 1 minor, 2 major (2/40=5%), and 0 very major errors, which was not acceptable. *K. oxytoca* had an EA of 87.8% and CA of 95.9% with 0 minor, 1 major (1/47=2.1%), and 1 (1/2=50%) very major errors. Analysis of performance of *K. oxytoca* using a truncated lower reporting range ($\leq$0.25 µg/mL - $\geq$128 µg/mL) improved the EA to 95.9%. The 1 very major error reported with *K. oxytoca* was considered a random error due to the limited number of resistant isolates tested. This performance was acceptable. *K. pneumoniae* had an EA of 89.4% and CA of 98.6% with 2 minor, 0 major, and 0 very major errors, which was acceptable. *S. marcescens* had an EA of 89.7% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was acceptable. Due to the unacceptable performance for *C. freundii, C. koseri*, and *K. aerogenes*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting of *C. freundii, C. koseri*, and *K. aerogenes* due to the unacceptable performance:

Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:
- Ceftazidime: *Citrobacter freundii, Citrobacter koseri, and Klebsiella aerogenes*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Klebsiella oxytoca, Proteus mirabilis, Proteus vulgaris*, and *Serratia marcescens* isolates.

A total of 64 *P. aeruginosa* isolates were evaluated with ceftazidime. The combined results from clinical and challenge testing demonstrated an EA of 87.5% and CA of 96.9%. There were 0 major and 2 very major (2/24 = 8.3%) errors. None of the 2 very major errors had an MIC value that was in essential agreement with the reference MIC value. Therefore, the adjusted very major error rate remained the same at 8.3%, which was not acceptable. Due to the unacceptable performance for *P. aeruginosa*, this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *P. aeruginosa* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Ceftazidime: *Pseudomonas aeruginosa*

Ceftazidime-Avibactam. A total of 640 Enterobacterales isolates (indicated species: 43 *C. freundii,* 42 *C. koseri,* 38 *E. cloacae,* 201 *E. coli*, 49 *K. aerogenes,* 50 *K. oxytoca,* 141 *K. pneumoniae*, 34 *P. mirabilis,* 22 *S. marcescens;* non-indicated species: 20 *P. vulgaris*) were evaluated with ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 83.8% and CA of 99.5%. There were 1 major and 2 very major errors. When evaluating results by individual species, *C. koseri* had an EA of 88.1% and CA of 100% with 0 major and 0 very major errors. Analysis of performance of *C. koseri* using a truncated reporting range (≤0.125 µg/mL - ≥64 µg/mL) improved the EA to 100%, which was acceptable. *E. coli* had an EA of 82.1% and CA of 99.5% with 0 major and 1 (1/6=16.7%) very major errors. The adjusted very major error rate was the same. This performance was unacceptable. *K. aerogenes* had an EA of 63.3% and CA of 100% with 0 major and 0 very major errors. This performance was not acceptable. *K. oxytoca* had an EA of 86% and CA of 100% with 0 major and 0 very major errors. Analysis of performance for *K. oxytoca* using a truncated lower reporting range (≤0.125 µg/mL- ≥64 µg/mL) improved the EA to 96%, which was acceptable. *K. pneumoniae* had an EA of 76.6% and CA of 100% with 0 major and 0 very major errors, which was unacceptable. *P. mirabilis* had 1(1/1=100%) very major error that was not changed with adjustment; however, it was considered a random error due to the limited number of resistant isolates tested. This performance was acceptable. Due to the unacceptable performance for *E. coli, K. aerogenes*, and *K. pneumoniae*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *E. coli*, *K. aerogenes,* and *K. pneumoniae* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Ceftazidime-avibactam: *Escherichia coli*, *Klebsiella aerogenes, Klebsiella pneumoniae*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex*, *Klebsiella oxytoca*, *Proteus mirabilis*, *Proteus vulgaris*, and *Serratia marcescens* isolates.

A total of 28 *P. aeruginosa* isolates were evaluated with ceftazidime-avibactam. The combined results from clinical and challenge testing demonstrated an EA of 100% and CA of 100%. There were 0 major and 0 very major errors. This performance was acceptable.

A limitation statement is included in the device labeling to address the lack of testing with resistant *Pseudomonas aeruginosa* isolates.

Ceftolozane-Tazobactam. A total of 668 Enterobacterales isolates (indicated species: 42 *C. koseri*, 202 *E. coli,* 65 *E. cloacae* complex*,* 49 *K. aerogenes,* 50 *K. oxytoca,* 142 *K. pneumoniae,* 34 *P. mirabilis,* 20 *P. vulgaris,* 22 *S. marcescens;* non-indicated species*:* 42 *C. freundii*) were evaluated with ceftolozane-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 71.7% and CA of 95.5%. There were 17 minor, 4 major, and 9 very major errors. When looking at % EA across species, *C. freundii, C. koseri, E. cloacae complex, E. coli, K. aerogenes, K. oxytoca,* and *K. pneumoniae* all had an EA below 80%, which was unacceptable. *S. marcescens* had an EA of 86.4% and a CA of 100%, which was unacceptable. When evaluating results for other species, *P. mirabilis* and *P. vulgaris*, did not have sufficient isolates tested, separately or combined, for support of ceftolozane-tazobactam performance on the ASTar System. Due to the unacceptable performance for *C. freundii*, *C. koseri, E. cloacae* complex, *E. coli, K. aerogenes*, and *K. oxytoca, K. pneumoniae,* and *S. marcescens* and limited number of *P. mirabilis* and *P. vulgaris* samples, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting due to the unacceptable or insufficient performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:
> - Ceftolozane-tazobactam: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*

A total of 64 *P. aeruginosa* isolates were evaluated with ceftolozane-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 89.1% and CA of 96.9%. There were 1 minor, 0 major, and 1 very major (1/6 = 16.7%) errors. The 1 very major error was considered random due to the limited number of resistant isolates tested. However, due to limited performance data to support ceftolozane-tazobactam overall, *P. aeruginosa* is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *P. aeruginosa* due to minimal overall supportive performance data with ceftolozane-tazobactam:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Ceftolozane-tazobactam: *Pseudomonas aeruginosa*

Ceftriaxone. A total of 717 Enterobacterales isolates (indicated species: 43 *C. freundii,* 62 *E. cloacae,* 202 *E. coli*, 49 *K. aerogenes,* 50 *K. oxytoca,* 141 *K. pneumoniae*, 89 *P. mirabilis,* 39 *S. marcescens;* non-indicated species*:* 42 *C. koseri*) were evaluated with ceftriaxone. The combined results from clinical and challenge testing demonstrated an EA of 75.6% and CA of 97.5%. There were 7 minor, 3 major, and 8 very major errors. When looking at % EA across species, *C. freundii, C. koseri, E. cloacae* complex*, E. coli, K. aerogenes, K. oxytoca,*

and *K. pneumoniae* all had an EA below 85%, which was unacceptable. When evaluating results for other species, *P. mirabilis* and *S. marcescens* did not have sufficient isolates, separately or combined, for support of ceftriaxone performance on the ASTar system. Due to the unacceptable performance for *C. freundii, C. koseri, E. cloacae* complex, *E. coli, K. aerogenes*, *K. oxytoca* and *K. pneumoniae* and limited number of *P. mirabilis* and *S. marcescens*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting due to the unacceptable or insufficient performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:
> - Ceftriaxone: C*itrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca*, *Klebsiella pneumoniae, Proteus mirabilis, Serratia marcescens*

Cefuroxime. A total of 563 Enterobacterales isolates (22 *C. koseri,* 65 *E. cloacae* complex*,* 202 *E. coli*, 49 *K. aerogenes,* 50 *K. oxytoca,* 141 *K. pneumoniae*, 34 *P. mirabilis*) were evaluated with cefuroxime. The combined results from clinical and challenge testing demonstrated an EA of 93.1% and CA of 94.3%. There were 24 major and 8 very major errors. When evaluating results by individual species, *C. koser*i had an EA of 86.4% and CA of 95.5% with 1 (1/21=4.8%) major error even after an adjustment assessment, which was not acceptable. *E. cloacae* complex had 7 (7/26=26.9%) major and 3 (3/39=7.7%) very major errors. Six of the 7 major errors and 2 of the 3 very major errors had an MIC value that was in essential agreement with the reference MIC value. Therefore, the adjusted major error rate and adjusted very major error rates were 3.9% (1/26) and 2.6% (1/39), respectively, which were not acceptable. *K. aerogenes* had an EA of 79.6% and CA of 87.8% with 4 (4/32=12.5%) major and 2 (2/17=11.8%) very major errors, which was unacceptable. *K. oxytoca* had 1 (1/46=2.2%) major and 1(1/4=25%) very major error. The 1 very major error was considered a random error due to the limited number of resistant isolates tested. This performance was acceptable. *E. coli* had 10 (10/132=7.6%) major and 2 (2/70=2.9%) very major errors. Nine of the 10 major errors and 1 of the 2 very major errors had an MIC value that was in essential agreement with the reference MIC value. Therefore, the adjusted major error rate and adjusted very major error rates were 0.8% (1/132) and 1.4% (1/70), respectively, which was acceptable. Due to the unacceptable performance for *C. koseri, E. cloacae* complex, and *K. aerogenes*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting due to the unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:
> - Cefuroxime: *Citrobacter koseri, Enterobacter cloacae* complex*, Klebsiella aerogenes*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Klebsiella oxytoca* and *Proteus mirabilis* isolates.

Ciprofloxacin. A total of 720 Enterobacterales isolates (27 *C. freundii*, 22 *C. koseri*, 65 *E. cloacae* complex*,* 202 *E. coli*, 49 *K. aerogenes*, 49 *K. oxytoca*, 142 *K. pneumoniae*, 90 *P. mirabilis*, 35 *P. vulgaris*, 39 *S. marcescens*) were evaluated with ciprofloxacin. The

combined results from clinical and challenge testing demonstrated an EA of 97.5% and CA of 96.0%. There were 21 minor, 6 major, and 2 very major errors. When evaluating results by individual species, *C. freundii* had an EA of 96.3% and CA of 88.9% (EA of evaluable was 87.5%), which was not acceptable. *E. coli* had 1 major (1/127=0.8%) and 1 very major errors (1/69=1.4%), which was acceptable. *K. oxytoca* had 1 (1/2=50%) very major error, which was considered a random error due to the limited number of resistant isolates tested. The performance was acceptable. Due to the unacceptable performance for *C. freundii*, this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *C. freundii* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:
> - Ciprofloxacin: C*itrobacter freundii*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter koseri, Enterobacter cloacae* complex*, Klebsiella aerogenes, Klebsiella oxytoca*, *Proteus vulgaris,* and *Serratia marcescens*.

A total of 28 *P. aeruginosa* isolates were evaluated with ciprofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 96.4% and CA of 82.1%. The EA of evaluable was 91.7%. There were 5 minor, 0 major and 0 very major errors. Overall, performance was acceptable.

A limitation statement is included in the device labeling to address limited testing with resistant *Pseudomonas aeruginosa* isolates.

Ertapenem. A total of 504 Enterobacterales isolates (43 *C. freundii,* 42 *C. koseri,* 38 *E. cloacae,* 48 *E. coli*, 49 *K. aerogenes,* 50 *K. oxytoca,* 141 *K. pneumoniae,* 34 *P. mirabilis*, 20 *P. vulgaris,* 39 *S. marcescens*) were evaluated with ertapenem. The combined results from clinical and challenge testing demonstrated an EA of 83.1% and CA of 95.0%. There were 15 minor, 2 major, and 8 very major errors. When looking at % EA across species, *C. freundii, E. cloacae* complex*, E. coli, K. oxytoca, K. pneumoniae* and *S. marcescens* all had an EA below 85%, which was unacceptable. *K. aerogenes* had an EA of 87.8% and CA of 95.9% with 2 minor errors, which was not acceptable. When evaluating results for other species, *C. koseri, P. mirabilis*, and *P. vulgaris* did not have sufficient isolates, separately or combined, for support of ertapenem performance on the ASTar system. Due to the unacceptable performance for *C. freundii, E. cloacae* complex*, E. coli, K. aerogenes, K. oxytoca, K. pneumoniae* and *S. marcescens* and limited number of *C. koseri, P. mirabilis,* and *P. vulgaris*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting due to the unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Ertapenem: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Serratia marcescens*

Gentamicin. A total of 646 Enterobacterales isolates (43 *C. freundii,* 22 *C. koseri,* 38 *E. cloacae,* 201 *E. coli*, 26 *K. aerogenes,* 30 *K. oxytoca,* 140 *K. pneumoniae,* 90 *P. mirabilis*, 34 *P. vulgaris,* 22 *S. marcescens*) were evaluated with gentamicin. The combined results from clinical and challenge testing demonstrated an EA of 94.9% and CA of 97.8%. There were 12 minor, 1 major, and 1 very major errors. *E. cloacae* complex had an EA of 86.8% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was not acceptable. *E. coli* had 2 minor, 0 major, and 1 (1/27=3.7%) very major errors, which was not acceptable. *K. aerogenes* had an EA of 88.5% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was not acceptable. Due to the unacceptable performance for *E. cloacae* complex*, E. coli,* and *K. aerogenes,* these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting due to the unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Gentamicin: *Enterobacter cloacae* complex*, Escherichia coli, and Klebsiella aerogenes*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter freundii, Citrobacter koseri*, *Klebsiella oxytoca*, *Proteus mirabilis, Proteus vulgaris*, and *Serratia marcescens* isolates.

A total of 64 *P. aeruginosa* were evaluated with gentamicin. The combined results from clinical and challenge testing demonstrated an EA of 93.8% and CA of 96.9%. There were 2 minor, 0 major, and 0 very major errors. Overall performance was acceptable.

A limitation statement is included in the device labeling to address the lack of testing with resistant *Pseudomonas aeruginosa* isolates.

Levofloxacin. A total of 683 Enterobacterales isolates (27 *C. freundii,* 42 *C. koseri,* 65 *E. cloacae*, 201 *E. coli*, 49 *K. aerogenes,* 50 *K. oxytoca,* 141 *K. pneumoniae,* 34 *P. mirabilis,* 35 *P. vulgaris,* 39 *S. marcescens*) were evaluated with levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 98.2% and CA of 95.0%. There were 29 minor, 3 major, and 2 very major errors. When evaluating results by individual species*, C. freundii* had an EA of 100% and CA of 85.2% with 4 minor errors. The EA of evaluable was 100%, which was acceptable. *K. oxytoca* had 1(1/2=50%) very major error; which was considered a random error due to the limited number of resistant isolates tested. The performance was acceptable.

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter freundii*, *Citrobacter koseri*, *Enterobacter cloacae* complex, *Klebsiella aerogenes*, *Klebsiella oxytoca*, *Proteus mirabilis*, *Proteus vulgaris*, and *Serratia marcescens* isolates.

A total of 28 *P. aeruginosa* isolates were evaluated with levofloxacin. The combined results from clinical and challenge testing demonstrated an EA of 92.9% and CA of 82.1%. There were 5 minor, 0 major, and 0 very major errors. The EA of the evaluable was 92.3%. Overall performance was acceptable.

A limitation statement is included in the device labeling to address the lack of testing with resistant *Pseudomonas aeruginosa* isolates.

Meropenem. A total of 46 *A. baumannii* isolates were evaluated with meropenem. The combined results from clinical and challenge testing demonstrated an EA of 95.7% and CA of 93.5%. There were 3 minor, 0 major, and 0 very major errors. Overall performance was acceptable.

A total of 494 Enterobacterales isolates (indicated species: 42 *C. freundii,* 42 *C. koseri,* 61 *E. cloacae* complex, 188 *E. coli*, 41 *K. oxytoca,* 29 *K. pneumoniae,* 29 *P. mirabilis,* 18 *P. vulgaris,* 21 *S. marcescens;* non-indicated species: 23 *K. aerogenes*) were evaluated with meropenem. The combined results from clinical and challenge testing demonstrated an EA of 83.8% and CA of 97.4%. There were 8 minor, 0 major, and 5 very major errors. When evaluating results by individual species, *C. freundii* had an EA of 85.7% and CA of 95.2% with 2 minor errors. Analysis of performance of *C. freundii* using a truncated lower reporting range (≤0.06 µg/mL - ≥128 µg/mL) improved the EA to 92.9%, which was acceptable. *E. cloacae* complex had an EA of 73.8% and CA of 90.2% with 5 minor, 0 major, and 1 (1/7=14.3%) very major errors, which was not acceptable. *E. coli* had an EA of 87.2% and CA of 97.9% with 1 minor, 0 major, and 3 (3/8=37.5%) very major errors. Restricting *E. coli* reporting at an MIC value of 0.5 µg/mL and 1 µg/mL mitigated three very major errors. Analysis of performance of *E. coli* using a truncated lower reporting range (≤0.06 µg/mL) improved the EA to 95.2%. This performance was acceptable. *K. aerogenes* had an EA of 87.0% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was not acceptable. *K. oxytoca* had an EA of 61.0% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was not acceptable. *K. pneumoniae* had an EA of 58.6% and CA of 96.6% with 0 minor, 0 major, and 1 (1/1=100%) very major errors, which was not acceptable. *P. mirabili*s had an EA of 89.7% with a CA of 100% with 0 minor, 0 major, and 0 very major errors, which was acceptable. *P. vulgaris* had 1 (1/1=100%) very major error, which was considered as random due to the limited number of resistant isolates tested. This performance was acceptable. Due to the unacceptable performance for *E. cloacae* complex*, K aerogenes, K. oxytoca,* and *K. pneumoniae*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation is included in the device labeling to address the *E. coli* very major errors and restrict reporting of *E. cloacae* complex*, K aerogenes, K. oxytoca,* and *K. pneumoniae* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Meropenem: *Escherichia coli* when ASTar MIC is 0.5 or 1 µg/mL due to 3 very major errors; *Enterobacter cloacae complex, Klebsiella aerogenes, Klebsiella oxytoca,* and *Klebsiella pneumoniae*

A limitation statement is included in the device labeling to address the lack of testing with resistant *Citrobacter freundii, Citrobacter koseri, Escherichia coli, Proteus mirabilis, Proteus vulgaris, Serratia marcescens* isolates.

A total of 24 *P. aeruginosa* isolates were evaluated with meropenem. The combined results from clinical and challenge testing demonstrated an EA of 91.7% and CA of 100%. There were 0 minor, 0 major, and 0 very major errors. Overall, performance was acceptable.

A limitation is included in the device labeling to address the lack of testing with resistant *Pseudomonas aeruginosa* isolates.

Meropenem-vaborbactam. A total of 683 Enterobacterales isolates (indicated species: 43 *C. freundii,* 42 *C. koseri,* 64 *E. cloacae* complex, 201 *E. coli*, 49 *K. aerogenes,* 50 *K. oxytoca,* 141 *K. pneumoniae,* 34 *P. mirabilis,* 39 *S. marcescens;* non-indicated species: 20 *P. vulgaris*) were evaluated with meropenem-vaborbactam. The combined results from clinical and challenge testing demonstrated an EA of 97.1% and CA of 99.0%. There were 7 minor, 0 major, and 0 very major errors. The performance is acceptable.

A limitation is included in the device labeling to address the lack of testing with resistant *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris,* and *Serratia marcescens*.

Piperacillin-Tazobactam. A total of 49 *A. baumannii* isolates were evaluated with piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 71.4% and CA of 89.8%. There were 5 minor errors, 0 major errors, and 0 very major error. Due to the unacceptable performance for *A. baumannii*, this drug/organism combination is not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting of *A. baumannii* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combinations:
> - Piperacillin-tazobactam: *Acinetobacter baumannii*

A total of 699 Enterobacterales isolates (indicated species: 42 *C. koseri,* 202 *E. coli,* 142 *K. pneumoniae,* 34 *P. mirabilis,* 35 *P. vulgaris,* 39 *S. marcescens;* non-indicated species: 43 *C. freundii,* 64 *E. cloacae* complex*,* 49 *K. aerogenes,* 49 *K. oxytoca*) were evaluated with piperacillin-tazobactam. The combined results from clinical and challenge testing demonstrated an EA of 91.7% and CA of 94.4%. There were 29 minor, 5 major, and 5 very major errors. When evaluating results by individual species, *C. freundii* had an EA of 86.1%, CA of 90.7% as well as 3 minor, 0 major, and 1 very major (1/11 = 9.1%) errors, which was not acceptable. *K. aerogenes* had an EA of 85.7% and CA of 91.8% with 4 minor, 0 major, and 0 very major errors, which was not acceptable. *K. oxytoca* had an EA of 87.8% and CA of 95.9% with 1 minor, 0 major, and 1 (1/2=50%) very major errors, which was not acceptable. *K. pneumoniae* had 10 minor, 1 major (1/81=1.2%), and 2 (2/54=3.7%) very major errors. Restricting *K. pneumoniae* reporting at an MIC value of 8 µg/mL mitigated two very major errors. This performance was acceptable*. E. coli* had 1 very major error (1/23=4.3%). Restricting *E. coli* reporting at an MIC value of 8 µg/mL mitigated the one very major error. This performance was acceptable. Due to the unacceptable performance of *C. freundii, K. aerogenes,* and *K. oxytoca*, these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to address the *E. coli* and *K. pneumoniae* very major errors and restrict reporting of *C. freundii, K. aerogenes,* and *K. oxytoca* due to unacceptable performance:

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

- Piperacillin-tazobactam: *Escherichia coli* and *Klebsiella pneumoniae* when the ASTar MIC is 8 µg/mL; *Citrobacter freundii, Klebsiella aerogenes, Klebsiella oxytoca*

A limitation is included in the device labeling to address the lack of testing with resistant *Citrobacter koseri, Proteus mirabilis, Proteus vulgaris,* and *Serratia marcescens* isolates.

Tigecycline. A total of 629 Enterobacterales isolates (43 *C. freundii*, 42 *C. koseri*, 65 *E. cloacae* complex, 200 *E. coli*, 49 *K. aerogenes*, 50 *K. oxytoca*, 141 *K. pneumoniae*, 39 *S. marcescens*) were evaluated with tigecycline. The combined results from clinical and challenge testing demonstrated an EA of 96.0% and CA of 97.5%. There were 14 minor, 0 major, and 2 very major errors. When evaluating results by individual species, *K. oxytoca* had 1 (1/1=100%) very major error, which was considered a random error due to the limited number of resistant isolates tested. This performance was acceptable. *S. marcescens* had 1 (1/3=33.3%) very major error, which was considered a random error due to the limited number of resistant isolates tested. This performance was acceptable.

A limitation is included in the device labeling to address the limited of testing with resistant *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae complex, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca*, *Klebsiella pneumoniae*, and *Serratia marcescens* isolates.

Tobramycin. A total of 472 Enterobacterales isolates (27 *C. freundii,* 42 *C. koseri,* 38 *E. cloacae* complex*,* 49 *E. coli*, 49 *K. aerogenes*, 50 *K. oxytoca*, 142 *K. pneumoniae*, 34 *P. mirabilis,*19 *P. vulgaris*, 22 *S. marcescens)* were evaluated with tobramycin. The combined results from clinical and challenge testing demonstrated an EA of 89.8% and CA of 93.9%. There were 26 minor, 1 major, and 2 very major errors. When evaluating results by individual species, *E. coli* had an EA of 89.8% and CA of 91.8% with 3 minor, 0 major, and 1 (1/6=16.7%) very major errors. The 1 very major error was considered random due to the limited number of resistance isolates tested. This performance was acceptable. *K. aerogenes* had an EA of 87.8% and CA of 98.0% with 1 minor, 0 major, and 0 very major errors, which was not acceptable. *K. oxytoca* had an EA of 76% and CA of 100% with 0 minor, 0 major, and 0 very major errors, which was not acceptable. *K. pneumoniae* had an EA of 90.9% with a CA of 88.7% with 14 minor, 1 (1/92=1.1%) major, 1 (1/39=2.6%) very major errors. The EA of the evaluable was 90.5%. Restricted reporting at 4 µg/mL mitigated the 1 very major error. The performance was acceptable. *P. vulgaris* had an EA of 79.0% and CA of 94.7% with 1 minor, 0 major, and 0 very major errors, which was not acceptable. Due to the unacceptable performance for *K. aerogenes, K. oxytoca*, and *P. vulgaris,* these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to address the *K. pneumoniae* very major error and to restrict reporting of *K. aerogenes, K. oxytoca*, and *P. vulgaris* due to unacceptable performance:

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

- Tobramycin: *Klebsiella pneumoniae* when the ASTar MIC is 4 µg/mL due to 1 very major error; *Klebsiella aerogenes, Klebsiella oxytoca, Proteus vulgaris*

A limitation is included in the device labeling to address the lack/limited of testing with resistant *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Proteus mirabilis,* and *Serratia marcescens* isolates.

A total of 64 *P. aeruginosa* isolates were evaluated with tobramycin. The combined results from clinical and challenge testing demonstrated an EA of 87.5% and CA of 98.4%. There were 1 minor, 0 major, and 0 very major errors. This performance was not acceptable. Due to the unacceptable performance for *P. aeruginosa*, this drug/organism combination is not indicated for use with the ASTar System. The following limitation is included in the device labeling to restrict reporting of *P. aeruginosa* due to unacceptable performance:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Tobramycin: *Pseudomonas aeruginosa*

Trimethoprim-sulfamethoxazole. A total of 756 Enterobacterales isolates (indicated species: 65 *E. cloacae,* 202 *E. coli*, 49 *K. aerogenes,* 50 *K. oxytoca,* 141 *K. pneumoniae*, 90 *P. mirabilis*, 35 *P. vulgaris;* non-indicated species: 43 *C. freundii*, 42 *C. koseri*, 39 *S. marcescens)* were evaluated with trimethoprim-sulfamethoxazole. The combined results from clinical and challenge testing demonstrated an EA of 94.6% and CA of 98.4%. There were 0 minor, 10 major, and 2 very major errors. When evaluating results by individual species, *C. freundii* had an EA of 88.4% and CA of 97.7% with 1 major error (1/37 = 2.7%), which was not acceptable. *E. coli* had 1 major (1/141=0.7%) and 1 very major errors (1/61 = 1.6%, which were acceptable. *P. mirabilis* had an EA of 88.9% and CA of 94.4% with 4 (4/71=5.6%) major and 1(1/19=5.2%) very major errors. The adjusted error rate remained the same for *P. mirabilis*, thus the performance and error rates were not acceptable. *K. pneumoniae* had 3 (3/86=3.5%) major and 0 very major errors. The adjusted error rate remained the same, which is not acceptable. A limitation will be added in the device labeling to perform alternate testing when a resistant result is obtained for *K. pneumoniae*. Due to the unacceptable performance for *C. freundii* and *P. mirabilis,* these drug/organism combinations are not indicated for use with the ASTar System. The following limitation statement is included in the device labeling to restrict reporting of *C. freundii* and *P. mirabilis*:

> Perform an alternative method of testing prior to reporting results for the following antibiotic/organism combination(s):
> - Trimethoprim-Sulfamethoxazole: *Citrobacter freundii, Proteus mirabilis*

There were three major errors with *K. pneumoniae* which were addressed by the following limitation in the device labeling:

- Trimethoprim-Sulfamethoxazole with *Klebsiella pneumoniae* 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.

A limitation is included in the device labeling to address limited testing with resistant *Citrobacter koseri*, *Klebsiella aerogenes, Klebsiella oxytoca,* and *Proteus vulgaris,* and *Serratia marcescens.*

Table 11. ASTar System –ASTar G-BC Kit Performance of Quantitative Assays

	Tot	No. EA	EA%	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA%	No. R or NS	No. S	min	maj	vmj
[a]Amikacin-*Acinetobacter baumannii* [Breakpoints (µg/mL: 16(S), 32(I), 64(R)]													
Challenge	34	33	97.1	31	30	96.8	30	88.2	8	26	4	0	0
Fresh	1	1	100	1	1	100	1	100	0	1	0	0	0
Fresh Seeded	14	10	71.4	12	8	66.7	11	78.6	3	9	2	1	0
Total	49	44	89.8	44	39	88.6	42	85.7	11	36	6	1	0
[a]Amikacin-Enterobacterales [Breakpoints (µg/mL: 16(S), 32(I), 64(R)]													
Challenge	319	298	93.4	297	276	92.9	316	99.1	5	310	3	0	0
Fresh	229	174	76.0	227	172	75.8	228	99.6	0	228	1	0	0
Fresh Seeded	187	165	88.2	172	150	87.2	184	98.4	1	181	3	0	0
Total	735	637	86.7	696	598	85.9	728	99.1	6	719	7	0	0
Amikacin-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 16(S), 32(I), 64(R)]													
Challenge	34	31	91.2	32	29	90.6	32	94.1	2	29	2	0	0
Fresh	16	15	93.8	16	15	93.8	16	100	0	16	0	0	0
Fresh Seeded	14	13	92.9	14	13	92.9	14	100	0	14	0	0	0
Total	64	59	92.2	62	57	91.9	62	96.9	2	59	2	0	0
Ampicillin-Enterobacterales [Breakpoints (µg/mL: 8(S), 16(I), 32(R)]													
Challenge	84	84	100	38	38	100	83	98.81	31	53	1	0	0
Fresh	129	123	95.35	64	58	90.62	125	96.9	63	66	2	2	0
Fresh Seeded	23	23	100	4	4	100	23	100	21	2	0	0	0
Total	236	230	97.46	106	100	94.34	231	97.88	115	121	3	2	0
[a]Ampicillin-Sulbactam-*Acinetobacter baumannii* [Breakpoints (µg/mL: 8(S), 16(I), 32(R)]													
Challenge	34	32	94.1	29	27	93.1	28	82.4	9	23	6	0	0
Fresh	1	1	100	1	1	100	1	100	0	1	0	0	0
Fresh Seeded	14	11	78.6	14	11	78.6	6	42.9	9	4	7	1	0
Total	49	44	89.8	44	39	88.6	35	71.4	18	28	13	1	0
Ampicillin-Sulbactam-Enterobacterales [Breakpoints (µg/mL: 8(S), 16(I), 32(R)]													
Challenge	206	203	98.5	149	146	98.0	193	93.7	52	139	13	0	0
Fresh	182	178	97.8	171	167	97.7	161	88.5	41	115	20	1	0
Fresh Seeded	99	93	93.9	73	67	91.8	85	85.9	47	38	14	0	0
Total	487	474	97.3	393	380	96.7	439	90.1	140	292	47	1	0
[a]Aztreonam-Enterobacterales [Breakpoints (µg/mL: 4(S), 8(I), 16(R)]													
Challenge	279	274	98.2	44	39	88.6	273	97.9	54	219	6	0	0
Fresh	212	203	95.8	38	29	76.3	200	94.3	29	175	10	0	2
Fresh Seeded	188	176	93.6	55	43	78.2	181	96.3	80	107	4	0	3
Total	679	653	96.2	137	111	81.0	654	96.3	163	501	20	0	5
[a]Aztreonam-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 8(S), 16(I), 32(R)]													
Challenge	34	30	88.2	27	23	85.2	26	76.5	15	14	7	0	1
Fresh	16	14	87.5	16	14	87.5	11	68.8	4	12	3	0	2
Fresh Seeded	14	12	85.7	14	12	85.7	12	85.7	3	10	1	0	1
Total	64	56	87.5	57	49	86.0	49	76.6	22	36	11	0	4
[a]Cefazolin-Enterobacterales [Breakpoints (µg/mL: 2(S), 4(I), 8(R)]													
Challenge	181	168	92.8	139	126	90.7	135	74.6	79	56	43	3	0
Fresh	104	89	85.6	83	68	81.9	77	74.0	38	52	19	7	1
Fresh Seeded	66	56	84.9	29	19	65.5	55	83.3	45	16	10	1	0
Total	351	313	89.2	251	213	84.9	267	76.1	162	124	72	11	1
[a]Cefepime-Enterobacterales [Breakpoints (µg/mL: 2(S), 4-8(I), 16(R)]													
Challenge	318	308	96.9	43	33	76.7	313	98.4	46	268	5	0	0
Fresh	230	220	95.7	33	23	69.7	221	96.1	21	200	8	1	0
Fresh Seeded	190	174	91.6	73	57	78.1	171	90	52	120	18	1	0
Total	738	702	95.1	149	113	75.8	705	95.5	119	588	31	2	0
Cefepime-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 8(S), - (I), 16(R)]													
Challenge	34	33	97.1	28	27	96.4	31	91.2	15	19	0	2	1
Fresh	16	14	87.5	16	14	87.5	13	81.3	4	12	0	1	2

	Tot	No. EA	EA%	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA%	No. R or NS	No. S	min	maj	vmj
Fresh Seeded	14	13	92.9	14	13	92.9	13	92.9	3	11	0	0	1
Total	64	60	93.8	58	54	93.1	57	89.1	22	42	0	3	4
[a]Cefotaxime-*Acinetobacter baumannii* Breakpoints (µg/mL: 8(S), 16-32(I), 64(R)]													
Challenge	34	27	79.41	23	16	69.57	32	94.12	32	0	2	0	0
Fresh	1	1	100	1	1	100	1	100	1	0	0	0	0
Fresh Seeded	14	14	100	6	6	100	14	100	14	0	0	0	0
Total	49	42	85.71	30	23	76.67	47	95.92	47	0	2	0	0
[a]Cefotaxime-Enterobacterales Breakpoints (µg/mL: 1(S), 2(I), 4(R)]													
Challenge	326	273	83.74	267	214	80.15	321	98.47	67	259	1	1	3
Fresh	227	195	85.9	203	171	84.24	224	98.68	43	183	1	0	2
Fresh Seeded	182	140	76.92	146	104	71.23	173	95.05	81	98	4	0	5
Total	735	608	82.72	616	489	79.38	718	97.69	191	540	6	1	10
[a]Ceftazidime-Avibactam-Enterobacterales [Breakpoints (µg/mL: 8(S), - (I), 16(R)]													
Challenge	270	252	93.3	123	105	85.4	269	99.6	17	253	0	0	1
Fresh	200	148	74	109	57	52.3	198	99	3	197	0	1	1
Fresh Seeded	170	136	80	119	85	71.4	170	100	1	169	0	0	0
Total	640	536	83.8	351	247	70.4	637	99.5	21	619	0	1	2
Ceftazidime-Avibactam-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 8(S), - (I), 16(R)]													
Challenge	12	12	100	12	12	100	12	100	1	11	0	0	0
Fresh	3	3	100	3	3	100	3	100	0	3	0	0	0
Fresh Seeded	13	13	100	13	13	100	13	100	0	13	0	0	0
Total	28	28	100	28	28	100	28	100	1	27	0	0	0
[a]Ceftazidime-*Acinetobacter baumannii* [Breakpoints (µg/mL: 8(S), 16(I), 32(R)]													
Challenge	34	30	88.2	24	20	83.3	30	88.2	15	18	4	0	0
Fresh	1	1	100	1	1	100	1	100	0	1	0	0	0
Fresh Seeded	13	13	100	4	4	100	11	84.6	10	2	2	0	0
Total	48	44	91.7	29	25	86.2	42	87.5	25	21	6	0	0
[a]Ceftazidime-Enterobacterales [Breakpoints (µg/mL: 4(S), 8 (I), 16(R)]													
Challenge	281	262	93.2	83	64	77.1	275	97.9	58	217	6	0	0
Fresh	212	168	79.3	106	62	58.5	204	96.2	31	178	5	2	1
Fresh Seeded	189	165	87.3	96	72	75	180	95.2	75	108	5	2	2
Total	682	595	87.2	285	198	69.5	659	96.6	164	503	16	4	3
[a]Ceftazidime-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 8(S), - (I), 16 R)]													
Challenge	34	30	88.2	29	25	86.2	33	97.1	17	17	0	0	1
Fresh	16	14	87.5	16	14	87.5	16	100	4	12	0	0	0
Fresh Seeded	14	12	85.7	13	11	84.6	13	92.9	3	11	0	0	1
Total	64	56	87.5	58	50	86.2	62	96.9	24	40	0	0	2
[a]Ceftolozane-Tazobactam-Enterobacterales [Breakpoints (µg/mL: 2(S), 4(I), 8(R)]													
Challenge	276	218	78.99	233	175	75.11	269	97.46	48	225	4	1	2
Fresh	211	137	64.93	203	129	63.55	204	96.68	8	203	1	2	4
Fresh Seeded	181	124	68.51	157	100	63.69	165	91.16	43	130	12	1	3
Total	668	479	71.71	593	404	68.13	638	95.51	99	558	17	4	9
[a]Ceftolozane-Tazobactam-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 4(S), 8(I), 16(R)]													
Challenge	34	32	94.12	30	28	93.33	33	97.06	6	27	0	0	1
Fresh	16	13	81.25	16	13	81.25	16	100	0	16	0	0	0
Fresh Seeded	14	12	85.71	14	12	85.71	13	92.86	0	13	1	0	0
Total	64	57	89.06	60	53	88.33	62	96.88	6	56	1	0	1
[a]Ceftriaxone-Enterobacterales [Breakpoints (µg/mL: 1(S), 2(I), 4(R)]													
Challenge	311	261	83.9	212	162	76.4	306	98.4	65	244	4	0	1
Fresh	228	152	66.7	190	114	60.0	222	97.4	42	185	1	2	3
Fresh Seeded	178	129	72.5	139	90	64.8	171	96.1	87	90	2	1	4
Total	717	542	75.6	541	366	67.7	699	97.5	194	519	7	3	8
[a]Cefuroxime-Enterobacterales [Breakpoints (µg/mL: 8(S), - (I), 16(R)]													
Challenge	216	204	94.4	136	124	91.2	208	96.3	69	147	0	5	3

	Tot	No. EA	EA%	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA%	No. R or NS	No. S	min	maj	vmj
Fresh	205	188	91.7	167	150	89.8	191	93.2	48	157	0	12	2
Fresh Seeded	142	132	93.0	71	61	85.9	132	93.0	82	60	0	7	3
Total	563	524	93.1	374	335	89.6	531	94.3	199	364	0	24	8
[a]Ciprofloxacin-Enterobacterales [Breakpoints (µg/mL: 0.25(S), 0.5(I), 1(R)]													
Challenge	307	304	99.0	25	22	88.0	301	98.1	49	252	6	0	0
Fresh	226	216	95.6	26	16	61.5	213	94.3	53	170	7	5	1
Fresh Seeded	187	182	97.3	44	39	88.6	177	94.7	55	123	8	1	1
Total	720	702	97.5	95	77	81.1	691	96.0	157	545	21	6	2
Ciprofloxacin-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 0.5(S), 1(I), 2(R)]													
Challenge	12	12	100	3	3	100	10	83.3	1	10	2	0	0
Fresh	3	2	66.7	2	1	50	2	66.7	0	2	1	0	0
Fresh Seeded	13	13	100	7	7	100	11	84.6	2	9	2	0	0
Total	28	27	96.4	12	11	91.7	23	82.1	3	21	5	0	0
[a]Ertapenem-Enterobacterales Breakpoints (µg/mL: 0.5(S), 1(I), 2(R)]													
Challenge	239	208	87.03	80	49	61.25	235	98.33	28	207	2	0	2
Fresh	110	97	88.18	38	25	65.79	104	94.55	4	103	3	2	1
Fresh Seeded	155	114	73.55	80	39	48.75	140	90.32	31	118	10	0	5
Total	504	419	83.13	198	113	57.07	479	95.04	63	428	15	2	8
[a]Gentamicin-Enterobacterales [Breakpoints (µg/mL: 4(S), 8(I), 16(R)]													
Challenge	281	265	94.3	238	222	93.3	276	98.2	26	254	5	0	0
Fresh	201	193	96.0	183	175	95.6	197	98.0	20	180	3	0	1
Fresh Seeded	164	155	94.5	135	126	93.3	159	97.0	11	150	4	1	0
Total	646	613	94.9	556	523	94.1	632	97.8	57	584	12	1	1
Gentamicin-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 4(S), 8(I), 16(R)]													
Challenge	34	31	91.2	30	27	90.0	32	94.1	7	25	2	0	0
Fresh	16	16	100	16	16	100	16	100	0	16	0	0	0
Fresh Seeded	14	13	92.9	14	13	92.9	14	100	1	13	0	0	0
Total	64	60	93.8	60	56	93.3	62	96.9	8	54	2	0	0
Levofloxacin-Enterobacterales [Breakpoints (µg/mL: 0.5(S), 1(I), 2(R)]													
Challenge	283	280	98.9	44	41	93.2	275	97.2	44	234	8	0	0
Fresh	213	208	97.7	54	49	90.7	203	95.3	42	167	7	2	1
Fresh Seeded	187	183	97.9	62	58	93.6	171	91.4	45	130	14	1	1
Total	683	671	98.2	160	148	92.5	649	95.0	131	531	29	3	2
Levofloxacin-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 1(S), 2(I), 4(R)]													
Challenge	12	11	91.7	10	9	90.0	10	83.3	1	10	2	0	0
Fresh	3	2	66.7	3	2	66.7	2	66.7	0	2	1	0	0
Fresh Seeded	13	13	100	13	13	100	11	84.6	2	9	2	0	0
Total	28	26	92.9	26	24	92.3	23	82.1	3	21	5	0	0
Meropenem-*Acinetobacter baumannii* [Breakpoints (µg/mL: 2(S), 4(I), 8(R)]													
Challenge	34	33	97.1	31	30	96.8	33	97.1	9	23	1	0	0
Fresh	1	1	100	1	1	100	1	100	0	1	0	0	0
Fresh Seeded	11	10	90.9	8	7	87.5	9	81.8	10	1	2	0	0
Total	46	44	95.7	40	38	95.0	43	93.5	19	25	3	0	0
[a]Meropenem-Enterobacterales [Breakpoints (µg/mL: 1(S), 2(I), 4(R)]													
Challenge	226	184	81.4	59	17	28.8	219	96.9	12	212	5	0	2
Fresh	142	127	89.4	17	2	11.8	141	99.3	1	141	0	0	1
Fresh Seeded	126	103	81.8	45	22	48.9	121	96.0	5	119	3	0	2
Total	494	414	83.8	121	41	33.9	481	97.4	18	472	8	0	5
Meropenem-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 2(S), 4(I), 8(R)]													
Challenge	12	10	83.3	11	9	81.8	12	100	1	11	0	0	0
Fresh	1	1	100	1	1	100	1	100	0	1	0	0	0
Fresh Seeded	11	11	100	11	11	100	11	100	0	10	0	0	0
Total	24	22	91.7	23	21	91.3	24	100	1	22	0	0	0
Meropenem-Vaborbactam-Enterobacterales [Breakpoints (µg/mL: 4(S), 8(I), 16(R)]													

	Tot	No. EA	EA%	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA%	No. R or NS	No. S	min	maj	vmj
Challenge	282	272	96.5	25	15	60.0	277	98.2	5	274	5	0	0
Fresh	212	210	99.1	2	0	0	211	99.5	1	210	1	0	0
Fresh Seeded	189	181	95.8	14	6	42.9	188	99.5	1	188	1	0	0
Total	683	663	97.1	41	21	51.2	676	99.0	7	672	7	0	0
[a]Piperacillin-Tazobactam-*Acinetobacter baumannii* [Breakpoints (µg/mL: 16(S), 32-64(I), 128(R)]													
Challenge	34	23	67.7	27	16	59.3	31	91.2	14	18	3	0	0
Fresh	1	0	0	1	0	0	1	100	0	1	0	0	0
Fresh Seeded	14	12	85.7	8	6	75.0	12	85.7	12	0	2	0	0
Total	49	35	71.4	36	22	61.1	44	89.8	26	19	5	0	0
[a]Piperacillin-Tazobactam-Enterobacterales [Breakpoints (µg/mL: 8(S), 16(I), 32(R)]													
Challenge	294	277	94.2	222	205	92.3	281	95.6	51	232	11	0	2
Fresh	213	194	91.1	207	188	90.8	201	94.4	12	194	8	3	1
Fresh Seeded	192	170	88.5	158	136	86.1	178	92.7	65	121	10	2	2
Total	699	641	91.7	587	529	90.1	660	94.4	128	547	29	5	5
Tigecycline-Enterobacterales [Breakpoints (µg/mL: 2(S), 4(I), 8(R)]													
Challenge	245	236	96.3	245	236	96.3	242	98.8	0	240	3	0	0
Fresh	206	196	95.2	206	196	95.2	202	98.1	1	203	4	0	0
Fresh Seeded	178	172	96.6	178	172	96.6	169	94.9	6	165	7	0	2
Total	629	604	96.0	629	604	96.0	613	97.5	7	608	14	0	2
[a]Tobramycin-Enterobacterales [Breakpoints (µg/mL: 4(S), 8(I), 16(R)]													
Challenge	222	200	90.1	217	195	89.9	211	95.1	23	194	11	0	0
Fresh	108	92	85.2	107	91	85.1	99	91.7	9	97	7	0	2
Fresh Seeded	142	132	93.0	141	131	92.9	133	93.7	17	114	8	1	0
Total	472	424	89.8	465	417	89.7	443	93.9	49	405	26	1	2
[a]Tobramycin-*Pseudomonas aeruginosa* [Breakpoints (µg/mL: 4(S), 8(I), 16(R)]													
Challenge	34	29	85.3	30	25	83.3	34	100	6	28	0	0	0
Fresh	16	14	87.5	16	14	87.5	16	100	0	16	0	0	0
Fresh Seeded	14	13	92.9	14	13	92.9	13	92.9	1	13	1	0	0
Total	64	56	87.5	60	52	86.7	63	98.4	7	57	1	0	0
[a]Trimethoprim-Sulfamethoxazole-Enterobacterales [Breakpoints (µg/mL: 2(S), - (I), 4(R)]													
Challenge	333	313	94.0	165	145	87.9	326	97.9	54	279	0	6	1
Fresh	230	223	97.0	76	69	90.8	228	99.1	52	178	0	1	1
Fresh Seeded	193	179	92.8	91	77	84.6	190	98.5	55	138	0	3	0
Total	756	715	94.6	332	291	87.6	744	98.4	161	595	0	10	2

[a]Due to unacceptable performance, do not report ASTar MIC results for certain drug/organism combinations. See limitations for details.

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

Trending

A trending analysis using combined clinical and challenge sample results was also conducted to evaluate antimicrobial-organism combinations for which ASTar MIC results were determined to be one or more doubling dilutions lower or higher than the reference result (**Table 12**). MIC results that were off-scale for both the reference and ASTar 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 12. ASTar System – ASTar BC C-Kit Trending

Drug	Organism Name	Total On Scale for Trending	≥1 Dilution Lower # (%)	Exact # (%)	≥1 Dilution Higher # (%)	Percent Difference (95% CI)	Significant Trending Noted
Amikacin	*Pseudomonas aeruginosa*	64	28 (43.75)	27	9 (14.06)	-30% (-43%, -14%)	Yes
Amikacin	*Citrobacter freundii*	27	14 (51.85)	10	3 (11.11)	-41% (-60%, -16%)	Yes
Amikacin	*Citrobacter koseri*	34	13 (38.24)	14	7 (20.59)	-18% (-37%, 4%)	No
Amikacin	*Enterobacter cloacae complex*	63	6 (9.52)	28	29 (46.03)	37% (21%, 50%)	Yes
Amikacin	*Klebsiella aerogenes*	47	7 (14.89)	30	10 (21.28)	6% (-9%, 22%)	No
Amikacin	*Klebsiella oxytoca*	49	7 (14.29)	27	15 (30.61)	16% (0%, 32%)	No
Amikacin	*Klebsiella pneumoniae*	135	16 (11.85)	80	39 (28.89)	17% (7%, 26%)	No
Amikacin	*Proteus mirabilis*	89	23 (25.84)	50	16 (17.98)	-8% (-20%, 4%)	No
Amikacin	*Serratia marcescens*	39	14 (35.9)	23	2 (5.13)	-31% (-47%, -13%)	Yes
Ampicillin	*Escherichia coli*	94	5 (5.32)	57	32, (34.04)	29% (18%, 39%)	No
Ampicillin	*Proteus mirabilis*	14	3 (21.43)	2	9 (64.29)	43% (6%, 67%)	Yes
Ampicillin Sulbactam	*Escherichia coli*	184	18 (9.78)	113	53 (28.8)	19% (11%, 27%)	No
Ampicillin Sulbactam	*Klebsiella oxytoca*	48	2 (4.17)	27	19 (39.58)	35% (19%, 50%)	Yes
Ampicillin Sulbactam	*Klebsiella pneumoniae*	97	9 (9.28)	44	44 (45.36)	36% (24%, 47%)	Yes
Ampicillin Sulbactam	*Proteus mirabilis*	12	4 (33.33)	4	4 (33.33)	0% (-34%, 34%)	No
Ampicillin Sulbactam	*Proteus vulgaris*	20	18 (90)	2	0 (0)	-90% (-97%, -64%)	Yes
Aztreonam	*Citrobacter koseri*	1	0 (0)	1	0 (0)	0% (-79%, 79%)	No
Aztreonam	*Enterobacter cloacae complex*	20	7 (35)	7	6 (30)	-5% (-32%, 23%)	No
Aztreonam	*Klebsiella aerogenes*	16	5 (31.25)	3	8 (50)	19% (-14%, 47%)	No
Aztreonam	*Klebsiella oxytoca*	21	2 (9.52)	2	17 (80.95)	71% (43%, 85%)	Yes
Aztreonam	*Klebsiella pneumoniae*	18	5 (27.78)	2	11 (61.11)	33% (1%, 57%)	Yes
Aztreonam	*Proteus mirabilis*	0	0 (0)	0	0 (0)	0	NA
Aztreonam	*Proteus vulgaris*	1	1 (100)	0	0 (0)	-100% (-100%, 12%)	No
Aztreonam	*Serratia marcescens*	3	2 (66.67)	0	1 (33.33)	-33% (-72%, 32%)	No
Cefazolin	*Klebsiella pneumoniae*	77	4 (5.19)	28	45 (58.44)	53% (40%, 64%)	Yes
Cefepime	*Pseudomonas aeruginosa*	60	13 (21.67)	21	26 (43.33)	22% (5%, 37%)	No
Cefepime	*Citrobacter freundii*	11	5 (45.45)	4	2 (18.18)	-27% (-57%, 11%)	No

Drug	Organism Name	Total On Scale for Trending	≥1 Dilution Lower # (%)	Exact # (%)	≥1 Dilution Higher # (%)	Percent Difference (95% CI)	Significant Trending Noted
Cefepime	*Citrobacter koseri*	0	0 (0)	0	0 (0)	0	NA
Cefepime	*Escherichia coli*	46	13 (28.26)	11	22 (47.83)	20% (0%, 37%)	No
Cefepime	*Klebsiella aerogenes*	6	2 (33.33)	0	4 (66.67)	33% (-19%, 67%)	No
Cefepime	*Klebsiella oxytoca*	4	1 (25)	2	1 (25)	0% (-49%, 49%)	No
Cefepime	*Klebsiella pneumoniae*	48	10 (20.83)	13	25 (52.08)	31% (12%, 47%)	Yes
Cefepime	*Proteus mirabilis*	9	2 (22.22)	1	6 (66.67)	44% (-1%, 71%)	No
Cefepime	*Proteus vulgaris*	2	1 (50)	0	1(50)	0% (-57%, 57%)	No
Cefepime	*Serratia marcescens*	7	2 (28.57)	1	4 (57.14)	29% (-19%, 62%)	No
Ceftazidime Avibactam	*Pseudomonas aeruginosa*	28	2 (7.14)	12	14 (50)	43% (20%, 61%)	Yes
Ceftazidime Avibactam	*Citrobacter freundii*	28	4 (14.29)	7	17 (60.71)	46% (21%, 64%)	Yes
Ceftazidime Avibactam	*Citrobacter koseri*	18	0 (0)	3	15 (83.33)	83% (55%, 94%)	Yes
Ceftazidime Avibactam	*Enterobacter cloacae complex*	24	0 (0)	7	17 (70.83)	71% (47%, 85%)	Yes
Ceftazidime Avibactam	*Klebsiella oxytoca*	19	2 (10.53)	1	16 (84.21)	74% (44%, 86%)	Yes
Ceftazidime Avibactam	*Proteus mirabilis*	1	1 (100)	0	0 (0)	-100% (-100%, 12%)	No
Ceftazidime Avibactam	*Proteus vulgaris*	1	0 (0)	0	1 (100)	100% (-12%, 100%)	No
Ceftazidime Avibactam	*Serratia marcescens*	20	0 (0)	9	11 (55)	55% (29%, 74%)	Yes
Ceftazidime	*Enterobacter cloacae complex*	29	5 (17.24)	4	20 (68.97)	52% (27%, 69%)	Yes
Ceftazidime	*Klebsiella oxytoca*	10	1 (10)	1	8 (80)	70% (27%, 87%)	Yes
Ceftazidime	*Klebsiella pneumoniae*	57	5 (8.77)	12	40 (70.18)	61% (45%, 73%)	Yes
Ceftazidime	*Proteus mirabilis*	1	1 (100)	0	0 (0)	-100% (-100%, 12%)	No
Ceftazidime	*Proteus vulgaris*	0	0,0	0	0 (0)	0	NA
Ceftazidime	*Serratia marcescens*	19	1 (5.26)	4	14 (73.68)	68% (39%, 84%)	Yes
Cefuroxime	*Escherichia coli*	143	8 (5.59)	66	69 (48.25)	43% (33%, 51%)	Yes
Cefuroxime	*Klebsiella oxytoca*	43	1 (2.33)	13	29 (67.44)	65% (47%, 77%)	Yes
Cefuroxime	*Klebsiella pneumoniae*	81	3 (3.7)	23	55 (67.9)	64% (52%, 74%)	Yes
Cefuroxime	*Proteus mirabilis*	17	2 (11.76)	5	10 (58.82)	47% (15%, 68%)	Yes
Ciprofloxacin	*Pseudomonas aeruginosa*	13	2 (15.38)	1	10 (76.92)	62% (23%, 80%)	Yes

Drug	Organism Name	Total On Scale for Trending	≥1 Dilution Lower # (%)	Exact # (%)	≥1 Dilution Higher # (%)	Percent Difference (95% CI)	Significant Trending Noted
Ciprofloxacin	*Citrobacter koseri*	0	0,0	0	0 (0)	0	NA
Ciprofloxacin	*Enterobacter cloacae complex*	22	3 (13.64)	8	11 (50)	36% (9%, 58%)	Yes
Ciprofloxacin	*Escherichia coli*	20	2 (10)	4	14 (70)	60% (30%, 77%)	Yes
Ciprofloxacin	*Klebsiella aerogenes*	6	0 (0)	2	4 (66.67)	67% (13%, 90%)	Yes
Ciprofloxacin	*Klebsiella oxytoca*	3	1 (33.33)	1	1 (33.33)	0% (-53%, 53%)	No
Ciprofloxacin	*Klebsiella pneumoniae*	29	0 (0)	11	18 (62.07)	62% (41%, 77%)	Yes
Ciprofloxacin	*Proteus mirabilis*	8	1 (12.5)	2	5 (62.5)	50% (3%, 76%)	Yes
Ciprofloxacin	*Proteus vulgaris*	0	0 (0)	0	0 (0)	0	NA
Ciprofloxacin	*Serratia marcescens*	8	0 (0)	2	6 (75)	75 (28%, 93%)	Yes
Gentamicin	*Pseudomonas aeruginosa*	60	35 (58.33)	23	2 (3.33)	-55% (-67%, -40%)	Yes
Gentamicin	*Citrobacter freundii*	40	8 (20)	24	8 (20)	0% (-18%, 18%)	No
Gentamicin	*Citrobacter koseri*	4	1 (25)	1	2 (50)	25% (-32%, 66%)	No
Gentamicin	*Klebsiella oxytoca*	28	1 (3.57)	11	16 (57.14)	54% (31%, 70%)	Yes
Gentamicin	*Klebsiella pneumoniae*	114	26 (22.81)	41	47 (41.23)	18% (6%, 30%)	No
Gentamicin	*Proteus mirabilis*	88	24 (27.27)	53	11 (12.5)	-15% (-26%, -3%)	No
Gentamicin	*Proteus vulgaris*	34	14 (41.18)	12	8 (23.53)	-18% (-38%, 5%)	No
Gentamicin	*Serratia marcescens*	22	3 (13.64)	18	1 (4.55)	-9% (-29%, 10%)	No
Levofloxacin	*Pseudomonas aeruginosa*	26	2 (7.69)	11	13 (50)	42% (18%, 61%)	Yes
Levofloxacin	*Citrobacter freundii*	12	2 (16.67)	7	3 (25)	8% (-24%, 39%)	No
Levofloxacin	*Citrobacter koseri*	0	0 (0)	0	0 (0)	0	NA
Levofloxacin	*Enterobacter cloacae complex*	22	3 (13.64)	8	11 (50)	36% (9%, 58%)	Yes
Levofloxacin	*Escherichia coli*	58	4 (6.9)	29	25 (43.1)	36% (21%, 50%)	Yes
Levofloxacin	*Klebsiella aerogenes*	6	0 (0)	4	2 (33.33)	33% (-12%, 70%)	No
Levofloxacin	*Klebsiella oxytoca*	6	2 (33.33)	3	1 (16.67)	-17% (-56%, 30%)	No
Levofloxacin	*Klebsiella pneumoniae*	40	5 (12.5)	20	15 (37.5)	25% (6%, 42%)	No
Levofloxacin	*Proteus mirabilis*	5	1 (20)	1	3 (60)	40% (-16%, 73%)	No
Levofloxacin	*Proteus vulgaris*	1	0 (0)	1	0 (0)	0% (-79%, 79%)	No

Drug	Organism Name	Total On Scale for Trending	≥1 Dilution Lower # (%)	Exact # (%)	≥1 Dilution Higher # (%)	Percent Difference (95% CI)	Significant Trending Noted
Levofloxacin	*Serratia marcescens*	21	1 (4.76)	5	15 (71.43)	67% (39%, 82%)	Yes
Meropenem	*Acinetobacter baumannii*	40	8 (20)	21	11 (27.5)	8% (-11%, 26%)	No
Meropenem	*Pseudomonas aeruginosa*	24	7 (29.17)	15	2 (8.33)	-21% (-42%, 2%)	No
Meropenem	*Citrobacter freundii*	10	6 (60)	1	3 (30)	-30% (-60%, 12%)	No
Meropenem	*Citrobacter koseri*	0	0 (0)	0	0 (0)	0	NA
Meropenem	*Escherichia coli*	35	7 (20)	3	25 (71.43)	51% (29%, 67%)	Yes
Meropenem	*Proteus mirabilis*	9	9 (100)	0	0 (0)	-100% (-100%, -58%)	Yes
Meropenem	*Proteus vulgaris*	7	3 (42.86)	1	3 (42.86)	0% (-42%, 42%)	No
Meropenem	*Serratia marcescens*	7	0 (0)	0	7 (100)	100% (50%, 100%)	Yes
Meropenem Vaborbactam	*Citrobacter freundii*	2	0, (0)	1	1 (50)	50% (-27%, 91%)	No
Meropenem Vaborbactam	*Citrobacter koseri*	0	0,0	0	0 (0)	0	NA
Meropenem Vaborbactam	*Enterobacter cloacae complex*	8	2 (25)	1	5 (62.5)	38% (-9%, 67%)	No
Meropenem Vaborbactam	*Escherichia coli*	10	4 (40)	2	4 (40)	0% (-37%, 37%)	No
Meropenem Vaborbactam	*Klebsiella aerogenes*	2	1 (50)	0	1 (50)	0% (-57%, 57%)	No
Meropenem Vaborbactam	*Klebsiella oxytoca*	1	1 (100)	0	0 (0)	-100% (-100%, 12%)	No
Meropenem Vaborbactam	*Klebsiella pneumoniae*	16	1 (6.25)	3	12 (75)	69% (36%, 84%)	Yes
Meropenem Vaborbactam	*Proteus mirabilis*	2	2 (100)	0	0 (0)	-100% (-100%, -7%)	Yes
Meropenem Vaborbactam	*Proteus vulgaris*	0	0 (0)	0	0 (0)	0	NA
Meropenem Vaborbactam	*Serratia marcescens*	3	0 (0)	0	3 (100)	100% (21%, 100%)	Yes
Piperacillin Tazobactam	*Citrobacter koseri*	42	1 (2.38)	15	26 (61.9)	60% (41%, 73%)	Yes
Piperacillin Tazobactam	*Enterobacter cloacae complex*	57	12 (21.05)	22	23 (40.35)	19% (2%, 35%)	No
Piperacillin Tazobactam	*Escherichia coli*	193	15 (7.77)	97	81 (41.97)	34% (26%, 42%)	Yes
Piperacillin Tazobactam	*Klebsiella pneumoniae*	106	16 (15.09)	26	64 (60.38)	45% (33%, 56%)	Yes
Piperacillin Tazobactam	*Proteus mirabilis*	16	7 (43.75)	5	4 (25)	-19% (-46%, 13%)	No
Piperacillin Tazobactam	*Proteus vulgaris*	12	4 (33.33)	5	3 (25)	-8% (-40%, 26%)	No
Piperacillin Tazobactam	*Serratia marcescens*	38	7 (18.42)	22	9 (23.68)	5% (-13%, 23%)	No
Tigecycline	*Citrobacter freundii*	43	28 (65.12)	13	2 (4.65)	-60% (-73%, -42%)	Yes

Drug	Organism Name	Total On Scale for Trending	≥1 Dilution Lower # (%)	Exact # (%)	≥1 Dilution Higher # (%)	Percent Difference (95% CI)	Significant Trending Noted
Tigecycline	*Citrobacter koseri*	42	6 (14.29)	33	3 (7.14)	-7% (-21%, 7%)	No
Tigecycline	*Enterobacter cloacae complex*	65	17 (26.15)	43	5 (7.69)	-18% (-31%, -6%)	No
Tigecycline	*Escherichia coli*	200	46 (23)	119	35 (17.5)	-6% (-13%, 2%)	No
Tigecycline	*Klebsiella aerogenes*	49	19 (38.78)	25	5 (10.2)	-29% (-44%, -12%)	No
Tigecycline	*Klebsiella oxytoca*	50	14 (28)	34	2 (4)	-24% (-38%, -10%)	No
Tigecycline	*Klebsiella pneumoniae*	141	69 (48.94)	69	3 (2.13)	-47% (-55%, -38%)	Yes
Tigecycline	*Serratia marcescens*	39	7 (17.95)	30	2 (5.13)	-13% (-28%, 2%)	No
Tobramycin	*Citrobacter freundii*	27	8 (29.63)	13	6 (22.22)	-7% (-30%, 16%)	No
Tobramycin	*Citrobacter koseri*	42	4 (9.52)	19	19 (45.24)	36% (17%, 52%)	Yes
Tobramycin	*Enterobacter cloacae complex*	38	3 (7.89)	13	22 (57.89)	50% (30%, 65%)	Yes
Tobramycin	*Escherichia coli*	48	11 (22.92)	21	16 (33.33)	10% (-8%, 28%)	No
Tobramycin	*Klebsiella pneumoniae*	137	36 (26.28)	49	52 (37.96)	12% (1%, 22%)	No
Tobramycin	*Proteus mirabilis*	34	5 (14.71)	17	12 (35.29)	21% (0%, 39%)	No
Tobramycin	*Serratia marcescens*	22	14 (63.64)	8	0 (0)	-64% (-80%, -38%)	Yes
Trimethoprim Sulfamethoxazole	*Enterobacter cloacae complex*	40	11 (27.5)	13	16 (40)	12% (-8%, 32%)	No
Trimethoprim Sulfamethoxazole	*Escherichia coli*	30	6 (20)	8	16 (53.33)	33% (9%, 53%)	Yes
Trimethoprim Sulfamethoxazole	*Klebsiella aerogenes*	32	14 (43.75)	12	6 (18.75)	-25% (-45%, -2%)	No
Trimethoprim Sulfamethoxazole	*Klebsiella oxytoca*	25	3 (12)	4	18 (72)	60% (33%, 76%)	Yes
Trimethoprim Sulfamethoxazole	*Klebsiella pneumoniae*	76	20 (26.32)	37	19 (25)	-1% (-15%, 12%)	No
Trimethoprim Sulfamethoxazole	*Proteus vulgaris*	24	2 (8.33)	9	13 (54.17)	46% (20%, 65%)	Yes

Analysis of trending indicated that ASTar 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:

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

- Amikacin: *Pseudomonas aeruginosa, Citrobacter freundii, Serratia marcescens*
- Ampicillin-Sulbactam: *Proteus vulgaris*
- Gentamicin: *Pseudomonas aeruginosa*
- Meropenem: *Proteus mirabilis*
- Meropenem-vaborbactam: *Proteus mirabilis*

- Tigecycline: *Citrobacter freundii, Klebsiella pneumoniae*
- Tobramycin: *Serratia marcescens*

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

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

- Ampicillin: *Proteus mirabilis*
- Amikacin: *Enterobacter cloacae* complex
- Ampicillin-Sulbactam: *Klebsiella oxytoca, Klebsiella pneumoniae*
- Aztreonam: *Klebsiella oxytoca*, *Klebsiella pneumoniae*
- Cefazolin: *Klebsiella pneumoniae*
- Cefepime: *Klebsiella pneumoniae*
- Ceftazidime: *Enterobacter cloacae* complex*, Klebsiella oxytoca, Klebsiella pneumoniae, Serratia marcescens*
- Ceftazidime-avibactam: *Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Klebsiella oxytoca, Serratia marcescens, Pseudomonas aeruginosa*
- Cefuroxime: *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis*
- Ciprofloxacin: *Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae, Proteus mirabilis, Serratia marcescens, Pseudomonas aeruginosa*
- Gentamicin: *Klebsiella oxytoca*
- Levofloxacin: *Enterobacter cloacae* complex*, Escherichia coli, Serratia marcescens, Pseudomonas aeruginosa*
- Meropenem: *Escherichia coli*, *Serratia marcescens*
- Meropenem-vaborbactam: *Klebsiella pneumoniae*, *Serratia marcescens*
- Piperacillin-tazobactam: *Citrobacter koseri, Escherichia coli, Klebsiella pneumoniae*
- Tobramycin: *Citrobacter koseri, Enterobacter cloacae* complex
- Trimethoprim-Sulfamethoxazole: *Escherichia coli, Klebsiella oxytoca, Proteus vulgaris*

Non-indicated species. As required under 511A(b)(2)(C)(ii)(I) of the Federal Food, Drug and Cosmetic Act, the following statement is included in the Precautions section of the device labeling to address testing and reporting 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 infections due to microorganisms outside of those found in the indications and usage in the drug label. The clinical significance of susceptibility information in those instances is unknown. The approved labeling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.

2. Matrix Comparison:

Blood Culture Bottle Compatibility Study

The ASTar System was designed to accept samples from the majority of positive BCBs and blood culture media types. To demonstrate the ability of the ASTar System to report accurate AST results from various blood culture bottle types, the performance of the system was evaluated with the following isolates: *Escherichia coli (x2), Klebsiella oxytoca, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Enterobacter cloacae complex, Serratia marcescens, K. aerogenes*, and *Acinetobacter baumannii*. These isolates represented the product panel and were selected to favor resistance phenotypes with as many on-scale MIC values as possible. Positive BCBs and negative control samples of each BCB type were run on the ASTar system. In total 11 different BCB types were evaluated. All ten (10) isolates were run in triplicates in the six aerobic bottles. Eight (8) isolates, excluding *A. baumannii* and *P. aeruginosa*, were run in triplicate in the five anaerobic bottles. The bottles were cultured until positive and run on the ASTar System within 16 hours.

Two methods were used to evaluate the data. First, results were evaluated for each antimicrobial by bottle type and by organism. The essential agreement (EA) was compared to reference MIC obtained by frozen broth microdilution according to CLSI M07 for each antimicrobial stratified by organism and were considered acceptable if an EA of ≥90% for each antimicrobial/bottle type.

Additionally, mode MIC values for each antimicrobial were compared across all bottle types. The percentage of MIC values within ±1 doubling dilution of the mode MIC for each antimicrobial/bottle was determined. The combined data from these two analyses are summarized in **Table 13** below. MIC values were within ±1 doubling dilution to the mode across all bottle types in 95% of all MICs evaluated, indicating that the ASTar System performed in EA with BMD and reproducibly across all bottle types.

At least one QC sample was run each day of testing. All QC strains were run each week for all instruments used in the study. All bottle types tested yielded MIC values within ±1 doubling dilution to the mode for >95% of all MIC results evaluated, indicating that the ASTar System performed similarly across all bottle types. Three bottles from each blood culture bottle type were also seeded with fresh human donor blood, but without bacteria, and incubated in the blood culture cabinet for at least 12 hours as a negative control. These negative samples did not complete the concentration adjustment step and were aborted by the instrument.

Table 13. Essential Agreement with BMD and Number of MIC Values ±1 to Mode Values across all Bottle Types for Non-Fastidious Antimicrobials in the ASTar BC G- Kit Panel

Blood Culture Bottle Type	Essential Agreement with BMD[a]	MIC values + 1 from mode value in all bottles/Total number of MIC values
BACT/ALERT FA Plus Aerobic	522/537 (97.2%)	539/540 (99.8%)
BACT/ALERT FN Plus Anaerobic	478/486 (98.4%)	488/489 (99.8%)
BACT/ALERT PF Plus Peds	533/537 (99.3%)	538/540 (99.6%)
BACT/ALERT SN Standard Anaerobic	480/486 (98.8%)	488/489 (99.8%)
BACT/ALERT SA Standard Aerobic	528/537 (98.3%)	534/540 (98.9%)

Blood Culture Bottle Type	Essential Agreement with BMD[a]	MIC values + 1 from mode value in all bottles/Total number of MIC values
BACTEC Peds Plus	534/537 (99.4%)	540/540 (100%)
BACTEC Lytic Anaerobic	477/486 (98.1%)	489/489 (100%)
BACTEC Plus Anaerobic	484/486 (99.6%)	489/489 (100%)
BACTEC Plus Aerobic	536/537 (99.8%)	539/540 (99.8%)
BACTEC Standard Aerobic	532/537 (99.1%)	539/540 (99.8%)
BACTEC Standard Anaerobic	481/486 (99.0%)	489/489 (100%)

[a]Essential Agreement <90% with BMD was observed for some combinations of antimicrobial/bottle type. For these combinations the individual isolates with results outside EA are specified below (numbers within parentheses show the ratio of replicates within EA/total). Tobramycin/BACTEC Standard Anaerobic: K. pneumoniae QM2403 (0/3); Cefotaxime/BACT/ALERT FA Plus Aerobic: E. coli QM2109 (1/3), K. oxytoca QM2400 (1/3); Tobramycin / BACT/ALERT FA Plus Aerobic: K. pneumoniae QM2403 (0/3), P. aeruginosa QM2231 (2/3), K. oxytoca QM2400 (2/3)

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:

Table 14. FDA-Approved or Recognized Interpretive Criteria[a]

Antimicrobial	Enterobacterales			*P. aeruginosa*			*Acinetobacter* spp.		
	S	I	R	S	I	R	S	I	R
Ampicillin	≤8	16	≥32	-	-	-	-	-	-
Ampicillin-sulbactam	≤8	16	≥32	-	-	-	-	-	-
Ceftazidime-avibactam	≤8	-	≥16	≤8	-	≥16	-	-	-
Meropenem-vaborbactam	≤4	8	≥16	-	-	-	-	-	-
Piperacillin-tazobactam	≤8	16	≥32	-	-	-	-	-	-
Cefazolin	≤2	4	≥8	-	-	-	-	-	
Cefepime	≤2	4-8	≥16	≤8	-	≥16	-	-	-
Cefuroxime	≤8	-	≥16	-	-	-	-	-	-
Ceftazidime	≤4	8	≥16	-	-	-	-	-	-

Aztreonam	≤4	8	≥16	-	-	-	-	-	-
Meropenem	≤1	2	≥4	≤2	4	≥8	≤2	4	≥8
Gentamicin	≤4	8	≥16	≤4	8	≥16	-	-	-
Tobramycin	≤4	8	≥16	-	-	-	-	-	-
Amikacin	≤16	32	≥64	≤16	32	≥64	-	-	-
Tigecycline	≤2	4	≥8	-	-	-	-	-	-
Ciprofloxacin	≤0.25	0.5	≥1	≤0.5	1	≥2	-	-	-
Levofloxacin	≤0.5	1	≥2	≤1	2	≥4	-	-	-
Trimethoprim-sulfamethoxazole	≤2	-	≥4	-	-	-	-	-	-

S = Susceptible; I = Intermediate; R = Resistant

[a]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:

N/A

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.