April 26, 2024

Q-linea AB
℅ Peter Trabold
Regulatory Affairs Specialist
MDC Associates, Inc.
48 Dunham Ridge Road
Suite 4000
Beverly, Massachusetts 01915

Re: K221688
Trade/Device Name: ASTar BC G- Kit and ASTar Instrument
Regulation Number: 21 CFR 866.1650
Regulation Name: A Cellular Analysis System For Multiplexed Antimicrobial Susceptibility Testing
Regulatory Class: Class II
Product Code: SAN, LON
Dated: November 15, 2023
Received: November 15, 2023

Dear Peter Trabold:

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

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

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

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

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

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

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

Sincerely,

Natasha Griffin -S

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

Enclosure

Indications for Use

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

510(k) Number *(if known)*
K221688

Device Name
ASTar BC G- Kit and ASTar Instrument

Indications for Use *(Describe)*

Intended 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.

Indications for Use:
The ASTar 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

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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8.0 510(k) Summary

Date of Submission: April 8th, 2024

Sponsor: Q-linea
Dag Hammarskjolds vag 52A
Uppsala, Sweden 752 37

Correspondent: MDC Associates, Inc.
Peter Trabold, Ph.D., MBA
48 Dunham Ridge Road, Suite 4000
Beverly, MA 01915
Phone: (978) 927 3808

8.1 Device

Name of Device: ASTar® BC G- Kit and ASTar® Instrument

Common Name: ASTar BC G- Kit and ASTar Instrument

Regulation Number: 21 CRF 866.1650

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

Regulatory Class: Class II

Product Code: SAN, LON

Predicate Device: Accelerate PhenoTest BC Kit. DEN160032

8.2 Device Description

ASTar System is a fully automated system for antimicrobial susceptibility testing (AST). It consists of the ASTar Instrument which is used in combination with dedicated application kits. The ASTar

BC G- Kit consists of the ASTar BC G- Consumable kit, ASTar BC G- Frozen insert, and ASTar BC G- Kit software which must be installed on the instrument to process the kit.

The system provides robust and consistent 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. Organism identification using an approved method is required to be entered into the ASTar Instrument for results to be reported.

The 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. The processed samples can be in different stages of the processing protocol. New samples can be loaded in a random-access manner when there are available slots. Processing of loaded samples will, in most cases, start shortly after loading. If six samples are started at the same time limitations given by the sample scheduler will result in a queue. The operator interacts with the instrument via the touchscreen display by which the operator controls the instrument.

ASTar BC G- Kit is used for *in vitro* determination of antimicrobial susceptibility testing of commonly isolated bacteria derived from positive blood culture samples confirmed positive for Gram-negative bacteria by Gram stain. The antimicrobial and organism combinations are listed in Table 1. Reportable ranges for each antimicrobial are listed in Table 2.

To start an analysis 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, from which the system purifies and quantifies the bacteria. The bacterial concentration is adjusted to the appropriate inoculum concentration and produces an inoculum for analysis of non-fastidious organisms. The bacterial suspensions are transferred automatically to the ASTar Disc and antimicrobial susceptibility testing is performed based on a defined short-term protocol. Results are available within approximately six hours. Bacterial growth and response to relevant concentrations of different antimicrobial drugs are measured throughout the incubation period, using a high-performance optical detection system in combination with image analysis algorithms. The system generates an MIC and further qualitative susceptibility results (i.e., S, I, R) for the tested antimicrobials when applicable. The qualitative results are determined based on established breakpoints stipulated by applicable authorities, i.e., FDA, CLSI or EUCAST. FDA Susceptibility Testing Interpretive Criteria (STIC), aka “breakpoints” are found in Table 3.

Table 1: ASTar BC G- Kit Product Panel

Antimicrobial class	Antimicrobial agent	*A. baumannii*	*C. freundii*	*C. koseri*	*E. cloacae* complex*	*E. coli*	*K. aerogenes*	*K. oxytoca*	*K. pneumoniae*	*P. aeruginosa*	*P. mirabilis*	*P. vulgaris*	*S. marcescens*
Penicillins	Ampicillin					●					●		
β-lactam combination agents	Ampicillin-sulbactam					●		●	●		●	●	
β-lactam combination agents	Ceftazidime-avibactam		●	●	●			●		●	●		●
β-lactam combination agents	Meropenem-vaborbactam		●	●	●	●	●	●	●		●		●
β-lactam combination agents	Piperacillin-tazobactam			●		●			●		●	●	●
Cephalosporin	Cefazolin								●				
Cephalosporin	Cefepime		●			●	●	●	●	●	●	●	●
Cephalosporin	Cefuroxime					●		●	●		●		
Cephalosporin	Ceftazidime				●	●		●	●		●	●	●
Monobactam	Aztreonam			●	●	●	●	●	●		●	●	●
Carbapenem	Meropenem	●	●	●		●				●	●	●	●
Aminoglycoside	Gentamicin		●	●				●	●	●	●	●	●
Aminoglycoside	Tobramycin		●	●	●	●			●		●		●
Aminoglycoside	Amikacin		●		●		●	●	●	●	●		●
Tetracycline	Tigecycline		●	●	●	●	●	●	●				●
Fluoroquinolone	Ciprofloxacin			●	●	●	●	●	●	●	●	●	●
Fluoroquinolone	Levofloxacin		●	●	●	●	●	●	●	●	●	●	●
Miscellaneous	Trimethoprim-sulfamethoxazole				●	●	●	●	●			●	

**Enterobacter cloacae* complex includes *E. cloacae*, *E. asburiae* and *E. hormaechei*.

Table 2: Organisms Antimicrobial Reportable Ranges for AST and QC, Quality Control Strains and Acceptable Results. All concentrations are in µg/mL.

Antimicrobial	ASTar BC G- Reportable Range (AST)[5]	ASTar BC G- Reportable Range (QC)	*E. coli* ATCC 25922	*P. aeruginosa* ATCC 27853	*K. pneumoniae* ATCC 700603	*K. pneumoniae* ATCC BAA 2814
Ampicillin	≤1 to ≥128	≤0.5 to ≥128	2-8		>128[4]	
Ampicillin-sulbactam	≤1 to ≥128[3]	≤1 to ≥128	2-8		8-32	
Ceftazidime-avibactam	≤0.125 to ≥64	≤0.06 to ≥64		0.5-4	0.25-2	
Meropenem-vaborbactam	≤0.25 to ≥64	≤0.06 to ≥64		0.125-1		0.125-0.5
Piperacillin-tazobactam	≤0.25 to ≥512	≤0.125 to ≥512[1] ≤0.25 to ≥512[2]		1-8	8-32	
Cefazolin	≤0.25 to ≥32	≤0.125 to ≥32	1-4			
Cefepime	≤0.25 to ≥128	≤0.125 to ≥128		0.5-4		
Cefuroxime	≤1 to ≥128	≤0.5 to ≥128	2-8			
Ceftazidime	≤0.25 to ≥128	≤0.125 to ≥128[1] ≤0.25 to ≥128[2]		1-4	16-64	
Aztreonam	≤0.25 to ≥128	≤0.125 to ≥128		2-8		
Meropenem	≤0.06 to ≥128	≤0.03 to ≥128		0.125-1		
Gentamicin	≤0.25 to ≥64	≤0.25 to ≥64		0.5-2		
Tobramycin	≤0.06 to ≥64	≤0.06 to ≥64	0.25-1			
Amikacin	≤0.5 to ≥256	≤0.125 to ≥256	0.5-4			
Tigecycline	≤0.03 to ≥32	≤0.008 to ≥32	0.03-0.25			
Ciprofloxacin	≤0.125 to ≥16	≤0.06 to ≥16		0.125-1		
Levofloxacin	≤0.125 to ≥32	≤0.125 to ≥32		0.5-4		
Trimethoprim-sulfamethoxazole	≤0.06 to ≥16	≤0.03 to ≥16	≤0.5			

[1]QC Reportable range for *P. aeruginosa* ATCC 27853

[2]QC Reportable range for *K. pneumoniae* ATCC 700603

[3]Truncate lower reportable range for Ampicillin-sulbactam/*Proteus vulgaris* combination to 2 µg/mL

[4]ASTar will report ≥128 µg/mL as an acceptable result.

[5]The reference range was truncated to match the AST BC G- reportable range for the following: Aztreonam/*Klebsiella oxytoca*: ≤0.015 - ≥256 µg/mL to ≤0.25 - ≥128 µg/mL; Ceftazidime/*Escherichia coli*: ≤0.03 - ≥256 µg/mL to ≤0.25 - ≥128 µg/mL; Ceftazidime/*Klebsiella oxytoca*: ≤0.03 - ≥256 µg/mL to ≤0.25 - ≥128 µg/mL; Ceftazidime-avibactam/*Citrobacter koseri*: ≤0.015 - ≥128 µg/mL to ≤0.125 - ≥64 µg/mL; Ceftazidime-avibactam/*Klebsiella oxytoca*: ≤0.015 - ≥128 µg/mL to ≤0.125 - ≥64 µg/mL; Meropenem/*Citrobacter freundii*: ≤0.004 - ≥1024 µg/mL to ≤0.06 - ≥128 µg/mL; Meropenem/*Escherichia coli*: ≤0.004 - ≥1024 µg/mL to ≤0.06 - ≥128 µg/mL

Table 3: FDA Recognized Susceptibility Test Interpretive Criteria (STIC) / "Breakpoints" implemented in the kit software.

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	-	-	-	-	-	-

8.3 Intended Use/Indications for Use

Intended 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.

Indications for Use

The ASTar 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*

Special Conditions for Use Statements

- Rx – For Prescription Use Only

8.4 Comparison of Technological Characteristics with the Predicate Device

Description	**Q-linea AB** **ASTar BC G– Kit** K221688 (New Device)	**Accelerate Diagnostics, Inc.** **Accelerate PhenoTest BC Kit** DEN160032 (Predicate Device)
Product Code(s)	SAN, LON	PRH, NSU, PEO, PAM, PEN, LON
Primary Regulation	21 CFR 866.1650	21 CFR 866.1650
Device Class	II	II
Device Classification	Fully automated short-term incubation cycle antimicrobial susceptibility system	Positive Blood Culture Identification and AST Kit
Intended Use/ Indication 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 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

Description	**Q-linea AB** **ASTar BC G− Kit** K221688 (New Device)	**Accelerate Diagnostics, Inc.** **Accelerate PhenoTest BC Kit** DEN160032 (Predicate Device)
	The ASTar 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.	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.
Instrument Required	ASTar Instrument	Accelerate Pheno System
Blood Culture Types Tested	BD BACTEC: Standard/10 Aerobic, Anaerobic; Lytic/10 Anaerobic; PEDS PLUS, Plus	BD BACTEC: Standard/10 Aerobic, Anaerobic; Lytic/10 Anaerobic; PEDS PLUS, Plus

Description	**Q-linea AB** **ASTar BC G– Kit** K221688 (New Device)	**Accelerate Diagnostics, Inc.** **Accelerate PhenoTest BC Kit** DEN160032 (Predicate Device)
	Aerobic, Anaerobic BioMeriuex BacT/ALERT: Standard Aerobic, Anaerobic; Plus Aerobic, Anaerobic; PF Plus	Aerobic, Anaerobic BioMeriuex BacT/ALERT: Standard Aerobic, Anaerobic; Plus Aerobic, Anaerobic; PF Plus Versa TREK: REDOX 1 and 2
Antimicrobials Tested	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
Organisms Tested for Antimicrobial Susceptibility Testing	<u>Gram-Negative Bacteria:</u> *Acinetobacter baumannii* *Citrobacter freundii* *Citrobacter koseri* *Enterobacter cloacae* complex *Escherichia coli* *Klebsiella aerogenes* *Klebsiella oxytoca* *Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Proteus mirabilis* *Proteus vulgaris*	<u>Gram-Negative Bacteria:</u> *Acinetobacter baumannii* *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) *Enterobacter* spp. (i.e., *Enterobacter cloacae, Enterobacter aerogenes*, not differentiated) *Escherichia coli* *Klebsiella* spp. (i.e., *Klebsiella pneumoniae,*

Description	**Q-linea AB** **ASTar BC G– Kit** K221688 (New Device)	**Accelerate Diagnostics, Inc.** **Accelerate PhenoTest BC Kit** DEN160032 (Predicate Device)
	Serratia marcescens	*Klebsiella oxytoca*, not differentiated) *Proteus* spp. (i.e., *Proteus mirabilis, Proteus vulgaris*, not differentiated) *Pseudomonas aeruginosa* *Serratia marcescens* <u>Gram-Positive Bacteria:</u> *Staphylococcus aureus* *Staphylococcus lugdunensis* Coagulase-negative *Staphylococcus* species (i.e., *Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus capitis, Staphylococcus lugdunensis*, *Staphylococcus warnerii*, not differentiated), *Enterococcus faecalis* *Enterococcus faecium*
Similarities		
Technology	High-speed, time-lapse microscopy imaging	Similar
Sample Types	Positive Blood Culture	Same
Sample Prep	Direct from sample. No manual McFarland preparation required	Same
Results	Minimum Inhibitory Concentration (MIC) based Antimicrobial Susceptibility Testing direct from Positive Blood Cultures	Same
Differences		
Sample per Instrument	12 samples	1 sample

Description	**Q-linea AB** **ASTar BC G− Kit** K221688 (New Device)	**Accelerate Diagnostics, Inc.** **Accelerate PhenoTest BC Kit** DEN160032 (Predicate Device)
Types of Results Provided	Provides AST results only. ID is required but provided by alternative method	Provides both ID and AST
Types Organisms Tested	Provides AST results for Gram-negative bacteria only	Provides ID and AST results for both Gram-positive and Gram-negative bacteria
Time to AST Results	Approximately 6 hours	Approximately 7 hours

8.5 Performance Characteristics

The following performance data were provided in support of the substantial equivalence determination.

8.5.1 Reproducibility

Reproducibility studies of the ASTar System (ASTar BC G− Kit run on ASTar Instrument) for positive Gram-negative blood culture bottles, BCBs, included the evaluation of 23 bacterial strains to obtain at least six on-scale MIC values for each antimicrobial. Triplicate samples from each contrived blood culture were tested at three separate sites on at least two separate days (supplementary testing was conducted in-house with three individual instruments). Thus at least six samples for each isolate were tested at each site and each isolate yielded a minimum of 18 results (3 sites x 2 days x 3 replicates). In total, all samples were tested within 16 hours of bottle positivity.

Performance was compared between three sites, with test isolates that are analyzed on at least two separate days to assess inter-site reproducibility and intra-site reproducibility of the ASTar System. The system needed to demonstrate an overall reproducibility of ≥ 95% based on the number of results that fall within ±1 doubling dilution between the test MIC result and test MIC mode. Reproducibility was calculated for both best-case scenario (assumes any off-scale results are within one dilution from the adjacent on-scale result) and worst-case scenario (assumes any off-scale results are more than one dilution from the adjacent on-scale result).

In the initial reproducibility study, inter-site reproducibility was evaluated at three sites and the results are summarized in Table 4. A supplemental reproducibility study was performed with

three instruments at a single internal site. The aggregated results from the initial and supplementary study are summarized in Table 5.

Table 4. Summary of initial and supplemental reproducibility results from all sites for ASTar BC G- Kit (by study).

Antimicrobial	Initial reproducibility testing		Supplementary testing	
	Best-case[1] (%)	Worst-case[2] (%)	Best-case[1] (%)	Worst-case[2] (%)
Amikacin	144/144 (100%)	139/144 (96.5%)	53/53 (100%)	53/53 (100%)
Ampicillin	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%)	0/0 (N/A)[3]	0/0 (N/A)[3]
Cefazolin[4]	126/126 (100%)	126/126 (100%)	36/36 (100%)	36/36 (100%)
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%)	79/89 (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%)
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%)	36/36 (100%)	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)[5]	0/0 (N/A)[5]

[1] Best case scenario calculation for reproducibility assuming the off-scale result is within one well from the mode.
[2] Worst case scenario calculation for reproducibility assuming the off-scale result is greater than one well from the mode.
[3] After panel alteration the on-scale isolates used for supplemental testing were no longer included in the panel**.**
[4] Reproducibility results are based on testing with indicated species, but not claimed, due to panel alteration after the study was completed.
[5] No isolates with on-scale results for Trimethoprim-sulfamethoxazole were included in the supplementary testing.

All antimicrobials show a reproducibility of ≥ 95% for best-case scenario calculations. For worst-case scenario calculations all antimicrobials show reproducibility above 89% except two that were slightly below, Ceftazidime 88% and Ceftazidime-avibactam 88.8%. Two antimicrobials (Cefazolin and Meropenem) show reproducibility results based on testing with indicated species, but not claimed, due to panel alteration after reproducibility study completion see Table 5 for additional information.

Table 5. Summary of all reproducibility results from all sites for ASTar BC G- Kit.

Antimicrobial	Best case[1]	Worst case[2]
Amikacin	197/197 (100%)	192/197 (97.5%)
Ampicillin	154/162 (95.1%)	154/162 (95.1%)
Ampicillin-sulbactam	198/198 (100%)	196/198 (99%)
Aztreonam	108/108 (100%)	99/108 (91.7%)
Cefazolin[3]	162/162 (100%)	162/162 (100%)
Cefepime	142/143 (99.3%)	142/143 (99.3%)
Ceftazidime	107/108 (99.1%)	95/108 (88%)
Ceftazidime-avibactam	107/107 (100%)	97/107 (90.7%)
Cefuroxime	161/161 (100%)	161/161 (100%)
Ciprofloxacin	197/197 (100%)	197/197 (100%)
Gentamicin	161/161 (100%)	161/161 (100%)
Levofloxacin	251/251 (100%)	241/251 (96%)
Meropenem[4]	72/72 (100%)	72/72 (100%)
Meropenem-vaborbactam	143/143 (100%)	143/143 (100%)
Piperacillin-tazobactam	286/286 (100%)	286/286 (100%)
Tigecycline	373/377 (98.9%)	373/377 (98.9%)
Tobramycin	350/359 (97.5%)	350/359 (97.5%)
Trimethoprim-sulfamethoxazole	180/180 (100%)	171/180 (95%)

[1] Best case calculation for reproducibility assuming any off-scale results are within one dilution from the adjacent on-scale result.
[2] Worst case calculation for reproducibility assuming any off-scale results are more than one dilution from the adjacent on-scale result.
[3] Reproducibility results are based on testing with indicated species, but not claimed, due to panel alteration after the study was completed.
[4]Meropenem reproducibility with all indicated species was 144/144 (100%) for best and worst case scenarios.

8.5.2 Blood Culture Bottle Compatibility

Ten (10) isolates were included in the study; *E. coli* (x2), *K. oxytoca*, *K. pneumoniae*, *P. aeruginosa*, *P. mirabilis*, *E. cloacae* complex, *S. marcescens*, *K. aerogenes* and *A. baumannii*. These isolates represent the ASTar BC G- Kit panel and were selected to favor resistance phenotypes to provide as many on-scale MIC values as possible. Table 6 lists the BCBs included in this study.

Table 6. Blood culture bottles evaluated for ASTar BC G- Kit.

Manufacturer	BCB Type
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 medium in plastic culture vials
BD	BACTEC Lytic Anaerobic medium in plastic culture vials
BD	BACTEC Plus Anaerobic medium in plastic culture vials
BD	BACTEC Plus Aerobic medium in plastic culture vials
BD	BACTEC Standard Aerobic medium in plastic culture vials
BD	BACTEC Standard Anaerobic medium in plastic culture vials

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 bacteria. The pass criteria were the overall essential agreement (EA) as compared to reference MIC obtained by frozen broth microdilution according to CLSI M07 and shall be ≥90% for each antimicrobial, stratified by bacteria. 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 were determined. The overall data from these two analyses are summarized in Table 7.

All bottle types had an MIC value within ±1 doubling dilution to the mode across all bottle types in >95% of all MICs evaluated, indicating that the ASTar System performed similarly across all bottle types.

Table 7. Overall 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[1]	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%)

Blood culture bottle type	Essential Agreement with BMD[1]	MIC values ±1 from mode value in all bottles / Total number of MIC values
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%)
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%)

[1]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)
Ceftazidime-avibactam / BACT/ALERT SN Standard Anaerobic: *K. aerogenes* QM2179 (0/3). One sample with this antimicrobial/organism/blood culture bottle combination was evaluated during the clinical study and the results were within essential agreement.
Cefotaxime / BACT/ALERT FN Plus Anaerobic: *K. oxytoca* QM2400 (0/3)

Lastly, 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. As expected, these bottles didn't turn positive in the cabinet, but were still run on the ASTar System to determine what would happen if a negative bottle was accidentally loaded onto the system. These samples did not complete the concentration adjustment step and were aborted by the instrument.

8.5.3 Sample Stability

The time to positivity of a blood culture is unpredictable and can vary from hours up to days in the incubator and can depend on factors such as organism, bacterial concentration at blood draw, concurrent antibiotic treatment, and bottle type. Nine (9) isolates from the following organisms were included in this study: *E. coli, K. oxytoca, K. pneumoniae, P. aeruginosa, P. mirabilis, E. cloacae, S. marcescens, C. koseri* and *A. baumannii*. These isolates represent the ASTar BC G- Kit panel and were selected to favor resistance phenotypes and to include as many on-scale MIC values as possible. All timepoints were tested in triplicate with all organisms. To assess the stability of positive BCBs prior to loading on the ASTar System, the initial samples were loaded on the ASTar System within one hour of bottle positivity and the stability samples were

stored at either room temperature or remained in the blood culture cabinet at 35 °C for an additional 16 to 24 hours until tested on the ASTar System. The MIC values from the 16-24 hours incubation conditions (room temperature and 35 °C) were compared to the mode MIC values obtained from the samples run within one hour after positivity, see Table 8. If the test MIC value was within ±1 doubling dilution from the initial value, then that MIC value passed, otherwise it failed.

Table 8. Stability of samples loaded to the ASTar System within different timeframes after BCB positivity for each time/incubation condition. The format is "number of MIC values ±1 from mode MIC values in initial sample/total MIC values" ("pass rate in %").[1]

	Room Temperature		35 °C	
Antimicrobial	**16-18 hours**	**>18-24 hours[2]**	**16-18 hours**	**>18-24 hours**
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%)

[1] Data also includes indicated species, but not claimed, due to panel alteration after the study was completed.
[2]One RT sample (AS503 *S. marcescens* HVI056) was loaded at 24 hours and 49 minutes after positivity. One initial sample and one RT sample (AS5056 and AS5059, *E. cloacae* QM336) were by mistake removed from blood culture cabinet and loaded in ASTar before turning positive. These samples were excluded from analysis and re-run with new BCB inoculations.

Pass/fail criteria were >95% of MIC values within ±1 doubling dilution of the mode MIC of initial samples (loaded <1 hour), which was reached for all time/incubation conditions. The number of MIC values ±1 doubling dilution to the mode value in the initial sample was 100% for 16–24 hours at room temperature and 99.6% for 16–24 hours at 35°C. Samples stored for up to 16 hours after

positivity at either room temperature or at 35 °C in a blood culture cabinet produce equivalent results to samples loaded into the ASTar System within 1-hour of positivity.

8.5.4 Interfering Substances

The ASTar System performance was evaluated with contrived positive BCB spiked with potentially interfering endogenous and exogenous substances at the concentrations indicated in Tables 9 and 10, respectively. All potentially interfering substances were tested with all three organisms included in this study: *E. coli*, *P. aeruginosa* and *A. baumannii*. Each organism was also tested without the potential interferent added and this serves as the control samples. All conditions were tested in triplicate. The MIC values obtained from the interferent samples were compared to the mode MICs obtained from the control samples. If a MIC value was within ±1 doubling dilution from the control value, then the sample passed.

Table 9. Potential endogenous interferents, clinically relevant concentration ranges and concentration tested for the ASTar BC G- Kit.

Potential Interferent	Concentration Tested	Clinically relevant concentration range	
Conjugated bilirubin	400 mg/L	Normal adult	0-2 mg/L
Gamma-globulin	50 g/L (plasma concentration)	Normal adult	7.0-16.0 g/L (serum concentration)
RBCs (Hemoglobin/Hematocrit)	20 g/dL	Normal adult	12-18 g/dL
		Anemia	<12 g/dL
WBCs	12,000 WBCs/µL	Normal adult	4500-11,000 WBC/µL
		Leukocytosis	>12,000 WBC/µL
		Leukopenia	<4000 WBC/µL
Platelets	400,000 PLTs/µL	Normal adult	150,000-400,000 PLTs/µL
		Thrombocytopenia	<150,000/µL

Table 10. Potential exogenous interferents and concentration tested for the ASTar BC G- Kit.

Potential Interferent	Concentration tested	Clinically relevant concentration
Intralipid	20 g/L	2 g/L
Sodium polyanethole sulfonate (SPS)	0.1% w/v (in bottle with blood)	0.04% w/v (in bottle with blood)
Heparin	3000 Units/L	1100 Units/L

No interference was observed with any of the eight endogenous or exogenous substances (Table 11). All evaluation categories had a pass rate of 100% except for RBCs (99.1%). The study results

suggest that none of the tested interferents reduces quantitative AST performance of positive G- blood cultures run on the ASTar System.

Table 11. Test results for each evaluated interfering substance are shown for non-fastidious isolates with pass rate (%) as compared to control mode MIC values for the ASTar BC G- Kit.

Potential Interferent	Number of MIC values ±1 from mode MIC values in control	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%

8.5.5 Interfering Antibiotics

To assess the potential interference of blood drawn from patients already on empiric antimicrobial therapy, contrived positive BCB samples with and without the antibiotics were run on the ASTar System. Three (3) classes of antibiotics present on the ASTar BC G- Kit panel were evaluated (cephalosporin, fluoroquinolone and carbapenem) and the specific antibiotics and test concentrations are indicated in Table 12. Even though it is recommended to use blood culture bottles (BCBs) with resins to remove any antibiotics that could potentially interfere with growth, both resin and non-resin bottles are commonly used for testing patient samples. To determine if the presence or absence of resins would affect any potential interference from the antibiotics, two different bottle types from two main suppliers were evaluated, one containing resins (BD BACTEC Plus Aerobic, plastic), and the other lacking resins (bioMérieux BACT/ALERT SA Standard Aerobic). Nine (9) different organisms were used in this study, *K. pneumoniae* (x4), *E. coli* (x4) and *P. aeruginosa* and due to different resistance patterns in these isolates, not all organisms were used in all experimental combinations, but all organisms were resistant to the potentially interfering antibiotic under evaluation. All applicable combinations were tested in triplicate. If the MIC value was within ±1 from the control value then that MIC value passed, otherwise it failed.

Table 12. Interfering antibiotics and concentration to be tested for the ASTar BC G- Kit.

Antibiotic	Antibiotic class	Test concentration	Highest concentration under therapeutic treatment
Cefotaxime	Cephalosporin	52.8 mg/dL	17.6 mg/dL
Ciprofloxacin	Fluoroquinolone	1.20 mg/dL	0.40 mg/dL
Meropenem	Carbapenem	33.90 mg/dL	11.30 mg/dL

All six potentially interfering antibiotics/BCB-combinations evaluated passed the acceptance criteria of >95% pass rate as compared to control samples without interfering antibiotics, see Table 13.

Table 13. Test results for each evaluated potentially interfering antibiotic are shown, with pass rate (%) as compared to control mode/median MIC values for the ASTar BC G- Kit.[1]

Interferent	BCB type	Number of MIC values ±1 from mode value in control / Total number of evaluated MIC values	Pass Rate
Cefotaxime	BD BACTEC Plus Aerobic	191/194	98.5%
	BACT/ALERT SA Standard Aerobic	192/192	100%
Ciprofloxacin	BD BACTEC Plus Aerobic	194/194	100%
	BACT/ALERT SA Standard Aerobic	189/195	96.9%
Meropenem	BD BACTEC Plus Aerobic	158/159	99.4%
	BACT/ALERT SA Standard Aerobic	152/158	96.2%

[1]Pass rates <90% was observed for some combinations of interferent / bottle type / antimicrobial. For these combinations the results are specified below (numbers within parenthesis show the ratio of passed replicates/total).
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)

Note that the BACTEC bottles contained resins whereas the BACT/ALERT bottles did not contain resins.

8.5.6 Carry Over and Cross Contamination

Carry over and cross contamination was evaluated in the ASTar System using two different isolates of *E. coli*, one susceptible and the other resistant to many of the antimicrobials on the

ASTar BC G- Kit panel. The resistant and susceptible isolates, from contrived positive BCBs, were run in an alternating fashion and lastly with a run of all susceptible isolate samples that served as a control for this study. In total, 14 susceptible samples were evaluated and no carry over or cross contamination was observed as evidenced by 99.7% pass rate (307/308) for the susceptible isolate MIC value. The MIC for the susceptible isolate for each antimicrobial must be within ±1 doubling dilution of the control mode MIC to pass. All six drawers on two different instruments were evaluated.

8.5.7 Set Inoculum for AST

A set inoculum study was performed to assess the accuracy of the ASTar System to measure and adjust the bacterial concentration of a positive BCB prior to AST. Contrived positive BCB from four different species of bacteria (*E. coli*, *P. aeruginosa*, *E. cloacae* and *K. aerogenes*) were evaluated across a 6-logarithmic dilution range in triplicate. Bacterial concentrations in positive Gram-negative BCB are reported to be in the range of 7.6×10^7 - 5×10^9 CFU/mL in most cases. For positive BCB and dilutions with a starting bacterial concentration >5 x 10^7 CFU/mL, the concentration was assessed and adjusted successfully by the ASTar System for 95.8% (23/24) of samples and 100% of those (23/23), produced an inoculum within the acceptance ranges for AST, see Table 14. Despite being below the range commonly observed in positive Gram-negative BCB, the ASTar System was able to assess and adjust the bacterial concentration in 75% (9/12) samples and accurately produce an inoculum within the acceptance ranges in 88.9% (8/9) of those samples. As expected, all dilutions with a concentration <5 x 10^6 CFU/mL were aborted by the ASTar System due to low bacterial concentration (36/36).

Table 14. Summary table of all 72 samples evaluated for the ASTar BC G- Kit. BCB input concentration range distribution of samples, completed concentration adjustment rate and ASTar Output Viable Count (CFU/mL) pass rate.

BCB Input Viable Count (CFU/mL)	Quantity	Completed Concentration Adjustment	ASTar Output Viable Count within Acceptance Range
≥ 5 x 10^9	0	0/0 (0%)	(0/0) N/A
5 x 10^8 to < 4.99 x 10^9	12	12/12 (100%)	12/12 (100%)
5 x 10^7 to < 4.99 x 10^8	12	11/12 (91.7%)	11/11 (100%)
5 x 10^6 to < 4.99 x 10^7	12	9/12 (75.0%)	8/9 (88.9%) [1]
< 5 x 10^6	36	0/36 (0%)	(0/0) N/A
Total	**72**	**32/72 (44.4%)**	**31/32 (96.9%)**

[1]The viable count for *K. aerogenes* QM409 sample AS1093 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.

8.5.8 Clinical Study

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 Micro-Dilution (BMD) results performed according to CLSI M07 11th Edition. 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.

This study encompasses two testing periods, an initial clinical testing phase whose generated data was submitted in K221668 and a supplemental testing phase in which additional data was generated in support of K221668. The initial study was conducted at four sites including three external clinical sites in the United States (US) and one internal site in Sweden. The supplemental testing phase was conducted at three sites including two of the original external clinical sites in the United States (US) and on internal site in Sweden.

The initial clinical testing phases first sample was enrolled and tested at the clinical sites on November 29, 2021, with the last sample enrolled and tested on May 21, 2022.

The supplemental clinical testing phases first sample was enrolled and tested at the clinical sites on January 23, 2023, with the last sample enrolled and tested on May 3, 2023.

Correspondingly, two separate testing phases occurred at the central reference BMD testing site. Within the initial phase, the first challenge isolate was tested on June 17, 2021, with the last isolate tested on April 25, 2022. Within the supplemental phase, the first isolate was tested on January 27, 2023, with the last isolate tested on April 21, 2023.

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. Pathogen identification results from a rapid ID method were used to enter the species ID into the ASTar Instrument to generate AST results. If rapid ID results were not available or if the results from the rapid ID

method did not provide a specific species on the ASTar BC G- panel, results from MALDI performed on isolates from the purity of the blood culture was used for input into ASTar. MALDI was performed on all isolates and if there was a discrepancy between the rapid ID results and MALDI, MALDI was used for the final organism identification.

Testing was performed during this study with the following blood culture bottle types: BacT/ALERT SA Standard Aerobic, BacT/ALERT SN Standard Anaerobic, BACTEC Lytic/10 Anaerobic/F Medium, BACTEC PEDS PLUS/F Medium, and BACTEC PLUS Aerobic/F Medium.

Results from ASTar BC G- Kit testing were 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 cannot be established with the second set of plates, the Median from all six plates was used.

A total of 1,068 samples were enrolled in the study, across Fresh PBC (positive blood cultures) and contrived positive blood culture 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 including 256 fresh, positive blood cultures, 223 contrived with clinical stock isolates and 401 contrived blood cultures with challenge isolates. 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, see Table 15.

Table 15. Instrument performance yielding a valid AST result.

ASTar AST Sample Results	n (%)
Valid Samples	933 (100%)
Samples with No AST Results[1]	26 (2.8%)
Inadequate data to estimate MIC	7 (0.8%)
Positive Control Failure	13 (1.4%)
Instrument Error	2 (0.2%)
Poor Growth	4 (0.4%)
Samples with Partial AST Results[2]	17 (1.8%)
Inadequate data to estimate MIC	17 (1.8%)

[1]25 out of 26 (96.2%) Samples with No AST Results were able to be resolved upon retesting.

[2]Samples with Partial AST Results are samples with one or more antimicrobials which were unable to be resulted and were not retested.

AST Performance

AST performance was generally assessed based on criteria outlined in the FDA Special Controls: Antimicrobial Susceptibility Test (AST) Systems - Class II Special Controls Guidance for Industry and FDA. This included assessment of Essential Agreement (EA) when comparted to frozen BMD, Category Agreement using FDA recognized susceptibility testing interpretive criteria (STIC), determination of number and rate of very major (VMJ), major (MAJ) and minor (MIN) discrepant results, as well as determination of essential agreement of evaluable results when appropriate.

Table 16 lists the overall AST performance for antimicrobials based on the final proposed panel in the intended use and incorporates concentration restricted reporting, ASTar reportable range truncations and truncations of the BMD reference range to the AST reportable range.

Table 16: Overall AST performance of antimicrobials.[1]

Antimicrobial	Group	Assessed	No. EA	EA %	Eval EA Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	No. S	MIN	MAJ	VMJ
Amikacin	Enterobacterales	460	436	94.78	442	418	94.57	455	98.91	4	447	5	0	0
Amikacin	*Pseudomonas aeruginosa*	64	59	92.19	62	57	91.94	62	96.88	2	59	2	0	0
Ampicillin	Enterobacterales	236	230	97.46	106	100	94.34	231	97.88	115	121	3	2	0
Ampicillin-sulbactam	Enterobacterales	445	434	97.53	348	338	97.13	399	89.66	138	252	45	1	0
Aztreonam	Enterobacterales	637	615	96.55	124	102	82.26	617	96.86	150	473	16	0	4
Cefazolin	*Klebsiella pneumoniae*	140	135	96.43	77	72	93.51	123	87.86	69	63	15	1	1
Cefepime	Enterobacterales	632	601	95.09	125	94	75.2	608	96.2	107	503	22	2	0
Cefepime	*Pseudomonas aeruginosa*	64	60	93.75	58	54	93.1	57	89.06	22	42	0	3	4
Ceftazidime	Enterobacterales	549	491	89.44	208	150	72.12	531	96.72	143	394	14	2	2
Ceftazidime-avibactam	Enterobacterales	229	212	92.58	109	92	84.4	227	99.13	7	222	0	1	1
Ceftazidime-avibactam	*Pseudomonas aeruginosa*	28	28	100	28	28	100	28	100	1	27	0	0	0
Cefuroxime	Enterobacterales	427	403	94.38	280	256	91.43	412	96.49	142	285	0	12	3
Ciprofloxacin	Enterobacterales	693	676	97.55	87	70	80.46	667	96.25	155	521	18	6	2
Ciprofloxacin	*Pseudomonas aeruginosa*	28	27	96.43	12	11	91.67	23	82.14	3	21	5	0	0
Gentamicin	Enterobacterales	381	363	95.28	320	302	94.38	370	97.11	29	347	10	1	0
Gentamicin	*Pseudomonas aeruginosa*	64	60	93.75	60	56	93.33	62	96.88	8	54	2	0	0
Levofloxacin	Enterobacterales	683	671	98.24	160	148	92.5	649	95.02	131	531	29	3	2
Levofloxacin	*Pseudomonas aeruginosa*	28	26	92.86	26	24	92.31	23	82.14	3	21	5	0	0
Meropenem	*Acinetobacter baumannii*	46	44	95.65	40	38	95	43	93.48	19	25	3	0	0
Meropenem	Enterobacterales	340	307	90.29	59	26	44.07	334	98.24	10	328	3	0	3
Meropenem	*Pseudomonas aeruginosa*	24	22	91.67	23	21	91.3	24	100	1	22	0	0	0
Meropenem-vaborbactam	Enterobacterales	663	643	96.98	41	21	51.22	656	98.94	7	652	7	0	0
Piperacillin-tazobactam	Enterobacterales	494	461	93.32	398	365	91.71	466	94.33	84	396	20	5	3
Tigecycline	Enterobacterales	629	604	96.03	629	604	96.03	613	97.46	7	608	14	0	2
Tobramycin	Enterobacterales	354	328	92.66	347	321	92.51	327	92.37	48	289	24	1	2
Trimethoprim-sulfamethoxazole	Enterobacterales	542	520	95.94	193	171	88.6	536	98.89	133	409	0	5	1

[1]EA performance (<90%) or other poor performance are addressed in limitation statements in the device labeling.

Overall, performance was generally high across most antimicrobials for EA, CA, VMJ rates and MAJ rates. This included both clinical samples (Fresh PBC and Stock) as well as samples with Challenge isolates. EA of Evaluable results was determined across all antimicrobials.

8.6 Conclusion

Conclusions drawn from the nonclinical and clinical tests (discussed above) demonstrate that the device is as safe, as effective, and the ASTar System was determined to be substantially equivalent to the predicate device (DEN160032).