September 15, 2020

Accelerate Diagnostics, Inc.
Carrene Plummer
Director, Regulatory Affairs
3950 S. Country Club Road #470
Tucson, Arizona 85714

Re: K192665
Trade/Device Name: Accelerate Pheno System, Accelerate PhenoTest BC Kit
Regulation Number: 21 CFR 866.1650
Regulation Name: Positive Blood Culture Identification and AST Kit
Regulatory Class: Class II
Product Code: PRH, NSU, PEO, PAM, PEN, LON
Dated: September 22, 2019
Received: September 25, 2019

Dear Carrene Plummer:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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

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

Sincerely,

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

Enclosure

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K192665

Device Name
Accelerate PhenoTest™ BC kit
Accelerate Pheno™ system

Indications for Use *(Describe)*
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.

The Accelerate PhenoTest™ BC kit identifies the following Gram-positive and Gram-negative bacteria and yeasts utilizing FISH probes targeting organism-specific ribosomal RNA sequences:

Staphylococcus aureus, Staphylococcus lugdunensis, Coagulase-negative Staphylococcus species (i.e., Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus capitis, Staphylococcus lugdunensis, Staphylococcus warneri, not differentiated), Enterococcus faecalis, Enterococcus faecium, Streptococcus spp. (i.e., Streptococcus mitis, Streptococcus oralis, Streptococcus gallolyticus, Streptococcus agalactiae, Streptococcus pneumoniae, not differentiated), Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated), Serratia marcescens, Candida albicans and Candida glabrata.

The Accelerate PhenoTest™ BC kit tests the following antimicrobial agents with the specific target organisms identified below:

Amikacin: Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Ampicillin: Enterococcus faecalis and Enterococcus faecium
Ampicillin/Sulbactam: Escherichia coli, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), and Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated)
Aztreonam: Pseudomonas aeruginosa, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Ceftazidime: Pseudomonas aeruginosa, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Ceftaroline: Staphylococcus aureus
Cefepime: Pseudomonas aeruginosa, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii,

Citrobacter koseri, not differentiated) and Serratia marcescens
Ceftriaxone: Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Ciprofloxacin: Pseudomonas aeruginosa, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Daptomycin: Staphylococcus aureus, Coagulase-negative Staphylococcus species (i.e., Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus capitis, Staphylococcus lugdunensis, Staphylococcus warneri, not differentiated), Enterococcus faecalis and Enterococcus faecium
Ertapenem: Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Gentamicin: Pseudomonas aeruginosa, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Linezolid: Staphylococcus aureus, Enterococcus faecalis and Enterococcus faecium
Meropenem: Pseudomonas aeruginosa, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Piperacillin/Tazobactam: Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Tobramycin: Pseudomonas aeruginosa, Klebsiella spp. (i.e., Klebsiella pneumoniae, Klebsiella oxytoca, not differentiated), Escherichia coli, Enterobacter spp. (i.e., Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes, not differentiated), Proteus spp. (i.e., Proteus mirabilis, Proteus vulgaris, not differentiated), Citrobacter spp. (i.e., Citrobacter freundii, Citrobacter koseri, not differentiated) and Serratia marcescens
Vancomycin: Staphylococcus aureus, Staphylococcus lugdunensis, Coagulase- negative Staphylococcus species (i.e., Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus capitis, Staphylococcus lugdunensis, Staphylococcus warneri, not differentiated), Enterococcus faecalis and Enterococcus faecium

The following resistance phenotype is reported based on qualitative tests: Methicillin-resistance (S. aureus S. lugdunensis, coagulase negative staphylococci).

The Accelerate PhenoTest™ BC kit is indicated as an aid in the diagnosis of bacteremia and fungemia. It is also indicated for susceptibility testing of specific pathogenic bacteria as identified above commonly associated with or causing bacteremia. Results are intended to be used in conjunction with other clinical and laboratory findings.

Standard laboratory protocols for processing positive blood cultures should be followed to ensure availability of isolates for supplemental testing as needed. Additionally, subculture of positive blood culture is necessary for the identification and susceptibility testing of: organisms not identified by the Accelerate PhenoTest™ BC kit, organisms present in polymicrobial samples, organisms for which species identification is critical for patient care (e.g. speciation of Streptococcus spp.), samples for which an “indeterminate” result for any probe was obtained, for testing antimicrobial agents not included on the Accelerate panel and for epidemiologic testing.

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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# 510(k) Summary

## 510(k) SUMMARY

### Submitter Information:

Submitter: Accelerate Diagnostics, Inc.

Address: 3950 S. Country Club Road #470 Tucson, AZ 85714

Establishment Registration No: 3010671651

Contact Person: Carrene Plummer

Phone: (520) 405-1462

Fax: (520) 269-6580

E-mail: cplummer@axdx.com

Date Prepared: September 22, 2019

### Name of Device and Classification:

Trade Name: Accelerate PhenoTest™ BC kit, Accelerate Pheno™ system

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

Product Code: PRH, NSU, PEO, PAM, PEN, LON

### Predicate Device:

Accelerate PhenoTest™ BC kit/Accelerate Pheno™ system (DEN160032)

## Device Description

### Assay Description

There are no changes to the description of the assays in the Accelerate PhenoTest™ BC kit description provided in DEN160032, except for updated time to result and addition of an optical filter to assist in removal of interfering sample debris.

The Accelerate PhenoTest™ BC kit contains a sample vial, a 48-channel disposable test cassette and a reagent cartridge. All identification (ID) and antimicrobial susceptibility testing (AST) is performed in individual flowcells of the test cassette. The reagent cartridge contains gel electrofiltration (GEF) stations, fluorescence *in situ* hybridization (FISH) probes, antimicrobials, and reagents for automated sample preparation, identification of bacterial and fungal target organisms, and antimicrobial susceptibility and resistance marker detection testing for bacterial target organisms. The user loads the sample into the sample vial, places the test cassette, reagent cartridge and sample vial into an Accelerate Pheno™ system module, then presses the module button to close the module door and start the run. The rest of the operations are automated as described below.

### Automated Sample Preparation

Automated sample preparation is performed using gel electrofiltration (GEF) which is based on gel electrophoresis principles. Sample is automatically transferred to a gel well containing pores smaller than bacterial or yeast cells. Application of an electric field causes lysed blood cells and/or other sample debris to pass into the gel wall while bacterial/yeast cells remain inside the gel well. The electric field is briefly reversed to dislodge bacterial/yeast cells from the gel wall prior to removal.

### Cell Capture

Following sample preparation, recovered cells are automatically pipetted into multiple flowcell channels of the test cassette. Conductive layers of transparent indium tin oxide (ITO) coat the top and bottom inner surfaces of each flowcell channel and act as electrodes. An additional cationic poly-L-lysine layer on the bottom of each flowcell acts as a capture surface. When a voltage is applied, the negatively-charged bacterial/yeast cells migrate to the positively-charged capture surface where they are captured prior to imaging.

**Fluorescence in situ Hybridization (FISH) for Identification**

Cocktails of ATTO-532 (green) fluorescently-labeled DNA probes bind to the ribosomal RNA of target organisms following permeabilization. Each cocktail also includes ATTO-647 (red) labeled universal bacterial probe that binds to the ribosomal RNA of all clinically relevant bacteria (bacterial ID channels) or universal eukaryotic probe that binds to the ribosomal RNA of all clinically relevant yeast (yeast ID channels). The system images each flowcell using a fluorescence and dark-field microscope with camera and a filter set that captures emission from the FISH ID probes at 532 nm, 647 nm and in dark-field. An additional filter, capturing emission at 720 nm – 760 nm, is utilized prior to FISH ID for removal of interfering sample debris. To further exclude debris, only dark-field objects colocalized with universal probe signal are included in analysis. Colocalization of target probe signal and universal probe signal identifies a target organism.

The software also quantitates the total number of organisms present in a sample using a nucleic acid stain in a separate control flowcell. Comparing the relative numbers of each target organism to the number of objects lit up by the universal probes allows the system to differentiate bacteria/yeast from debris. FISH ID results are reported approximately 2 hours after loading the sample, and the ID result determines the selection of appropriate antimicrobials for subsequent antimicrobial susceptibility testing.

**Morphokinetic Cellular Analysis (MCA) for Antimicrobial Susceptibility Testing (AST)**

The Accelerate Pheno™ system leverages Morphokinetic Cellular Analysis (MCA) technology to measure distinct morphokinetic features of live microbial cells responding to antimicrobials to generate susceptibility results.

MCA is a computer vision based analytical method that uses digital microscopy inputs and machine learning technology to observe individual live cells and microcolonies (or clones) and recognize patterns of change over time. This technology tracks and analyzes multiple morphological and kinetic changes of individual cells and microcolonies under a variety of conditions. These changes include morphokinetic features such as cell morphology, mass as measured by light intensity of a growing microcolony, division rate, anomalous growth patterns, and heterogeneity.

Prior to AST, the remaining sample is combined with growth media and undergoes a pre-growth step during the FISH ID assay to normalize growth rates. Following automated sample preparation, the cells are quantitated and dynamically diluted to the appropriate concentration for AST testing. The cells are then captured in flowcell channels and

immobilized when growth media containing single concentrations of each test antimicrobial are added to separate flowcell channels. The bacteria in each flowcell are imaged every 10 minutes for up to 4.5 hours, creating a time-lapse record of bacterial growth from individual progenitor cells into clones of daughter cells.

During this period, morphokinetic features are measured and used for analysis. The precise quantitative measurement of individual clone growth rate over time is a powerful indicator of antimicrobial efficacy. Onboard software algorithms derive minimum inhibitory concentration (MIC) values from the measured features, and apply appropriate expert rules for proper interpretation and reporting of categorical interpretations - S, I or R (susceptible, intermediate, or resistant).

The Accelerate Pheno™ system is designed to perform Accelerate PhenoTest™ BC kit identification (ID) of bacterial and yeast cells and antimicrobial susceptibility testing (AST) in approximately 7 hours directly from positive blood culture samples. Depending on the computer configuration, up to eight ID/AST modules can be operated concurrently. Analysis time may increase when four or more tests are performed on ID/AST modules simultaneously. Other factors, such as sample complexity, the number of organisms and/or antimicrobials available in the panel, may also increase time to result.

**Quality Control**

The Accelerate PhenoTest™ BC ID and AST QC tests automate the external QC testing procedure, removing the manual standardized inoculum preparation and manual dispensing of the McFarland standardized inoculum (0.5 for bacteria and 2.0 for fungi). This reduces the complexity of QC testing, eliminating the need for a clinical scientist to perform the test. Furthermore, the stability of the analyte is increased through the use of complementary sequences coupled to polymer microspheres for each of the target probes in the Accelerate PhenoTest™ BC kit.

As accessories to the Accelerate PhenoTest™ BC kit and Accelerate Pheno™ system, the Accelerate PhenoTest™ BC ID and AST QC tests have their own instructions for use.

**Instrument Description**

Changes to the instrument description provided in the de novo submission (DEN160032) include the addition of an alternate computing system (Interface PC/Analysis module) that supports up to 8 modules and change in time to result.

The Accelerate Pheno™ system is a fully-integrated in vitro diagnostic system comprised of one to eight ID/AST module(s), a computing system, touchscreen monitor and Accelerate Pheno™ system software for use with Accelerate PhenoTest™ kits. It is designed to perform identification (ID) of bacterial and yeast cells and antimicrobial susceptibility testing (AST) in approximately 7 hours directly from positive blood culture samples. Depending on the computer configuration, up to eight ID/AST modules can be operated concurrently. Analysis time may increase when four or more tests are initiated on ID/AST modules simultaneously. Other factors, such as sample complexity, the number of organisms and/or antimicrobials available in the assay kit panel, may also increase time to result.

Identification uses fluorescence in situ hybridization (FISH) and susceptibility testing uses microscopic observation of individual, live, growing bacterial cells in near real time (approximately every 10 minutes) in the presence of antimicrobial agents.

The Accelerate Pheno™ system is comprised of the following hardware:

- Accelerate Pheno™ system ID/AST modules (Up to 4 or 8 depending on computing system architecture)
- Computing system, either:
    - Control PC/Analysis PC setup (supports up to 4 ID/AST modules):
        - 1 Control PC
        - 1 Analysis PC
    - Interface PC/Analysis module setup (supports up to 8 ID/AST modules):
        - 1 Interface PC
        - 1 Analysis module
- Touchscreen monitor
- Keyboard
- Mouse
- Power cords
- Cables
- Uninterruptible Power Supply (1 UPS for up to 4 ID/AST modules and 1 UPS per computing system)

Each system contains up to 4 or 8 ID/AST modules (depending on computing system) and each ID/AST module can run one patient sample at a time. Each ID/AST module may be started or stopped at any time, independent of the other ID/AST modules.

**Software Description**

There are no changes to the description of the Accelerate Pheno™ system software provided in DEN160032. The Accelerate Pheno™ system uses web-based software that controls system functions. The software can be accessed via the touchscreen monitor interface or remotely on a computer or device that has a web browser with network access to the host PC.

**Intended Use/Indications for Use**

The following changes have been made to the intended use/indications for use of the Accelerate PhenoTest™ BC kit since DEN160032: addition of the *Pseuodomonas aeruginosa* aztreonam assay, addition of newly recognized nomenclature for *Enterobacter aerogenes*, removal of macrolide-lincosamide-streptogramin B resistance (MLSb), and removal of erythromycin.

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.

The Accelerate PhenoTest™ BC kit identifies the following Gram-positive and Gram-negative bacteria and yeasts utilizing FISH probes targeting organism-specific ribosomal RNA sequences:

*Staphylococcus aureus*, *Staphylococcus lugdunensis*, Coagulase-negative S*taphylococcus* species (i.e., *Staphylococcus epidermidis, Staphylococcus haemolyticus*, *Staphylococcus hominis, Staphylococcus capitis, Staphylococcus lugdunensis, Staphylococcus warneri*, not differentiated), *Enterococcus faecalis, Enterococcus faecium, Streptococcus* spp. (i.e., *Streptococcus mitis, Streptococcus oralis, Streptococcus gallolyticus, Streptococcus agalactiae, Streptococcus pneumoniae*, not differentiated), *Pseudomonas aeruginosa*, *Acinetobacter baumannii, Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis, Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*,

*Citrobacter koseri*, not differentiated), *Serratia marcescens, Candida albicans* and *Candida glabrata.*

The Accelerate PhenoTest™ BC kit tests the following antimicrobial agents with the specific target organisms identified below:

Amikacin: *Pseudomonas aeruginosa*, *Acinetobacter baumannii, Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), Proteus *spp*. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Ampicillin: *Enterococcus faecalis* and *Enterococcus faecium*

Ampicillin/Sulbactam: *Escherichia coli, Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), and *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated)

Aztreonam: *Pseudomonas aeruginosa*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae*, *Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Ceftazidime: *Pseudomonas aeruginosa*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Ceftaroline: *Staphylococcus aureus*

Cefepime: *Pseudomonas aeruginosa*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Ceftriaxone: *Klebsiella* spp. (i.e., *Klebsiella pneumoniae*, *Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus*

*mirabilis, Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Ciprofloxacin: *Pseudomonas aeruginosa*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae, Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Daptomycin: *Staphylococcus aureus*, Coagulase-negative *Staphylococcus* species (i.e., *Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis*, *Staphylococcus capitis*, *Staphylococcus lugdunensis*, *Staphylococcus warneri*, not differentiated), *Enterococcus faecalis* and *Enterococcus faecium*

Ertapenem: *Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis, Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Gentamicin: *Pseudomonas aeruginosa*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Linezolid: *Staphylococcus aureus, Enterococcus faecalis* and *Enterococcus faecium*

Meropenem: *Pseudomonas aeruginosa*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae, Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Piperacillin/Tazobactam: *Pseudomonas aeruginosa, Acinetobacter baumannii*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae*, *Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Tobramycin: *Pseudomonas aeruginosa*, *Klebsiella* spp. (i.e., *Klebsiella pneumoniae*,

*Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (i.e., *Enterobacter cloacae*, *Enterobacter (Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (i.e., *Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (i.e., *Citrobacter freundii*, *Citrobacter koseri*, not differentiated) and *Serratia marcescens*

Vancomycin: *Staphylococcus aureus*, *Staphylococcus lugdunensis*, Coagulase-negative *Staphylococcus* species (i.e., *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Staphylococcus capitis*, *Staphylococcus lugdunensis*, *Staphylococcus warneri*, not differentiated), *Enterococcus faecalis* and *Enterococcus faecium*

The following resistance phenotype is reported based on a qualitative test: Methicillin-resistance (*S. aureus S. lugdunensis*, coagulase negative staphylococci).

The Accelerate PhenoTest™ BC kit is indicated as an aid in the diagnosis of bacteremia and fungemia. It is also indicated for susceptibility testing of specific pathogenic bacteria as identified above commonly associated with or causing bacteremia. Results are intended to be used in conjunction with other clinical and laboratory findings.

Standard laboratory protocols for processing positive blood cultures should be followed to ensure availability of isolates for supplemental testing as needed. Additionally, subculture of positive blood culture is necessary for the identification and susceptibility testing of: organisms not identified by the Accelerate PhenoTest™ BC kit, organisms present in polymicrobial samples, organisms for which species identification is critical for patient care (e.g. speciation of *Streptococcus* spp.), samples for which an "indeterminate" result for any probe was obtained, for testing antimicrobial agents not included on the Accelerate panel and for epidemiologic testing.

**Comparison of Technological Characteristics with the Predicate Device**

Table 1: Predicate Device Comparison Similarities

| Similarities | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| **Intended Use** | 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. | Same |

| Similarities | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| **Organisms Identified** | The Accelerate PhenoTest™ BC kit identifies the following Gram-positive and Gram-negative bacteria and yeasts utilizing FISH probes targeting organism-specific ribosomal RNA sequences: *Staphylococcus aureus*, *Staphylococcus lugdunensis*, Coagulase-negative S*taphylococcus* species (*Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Staphylococcus capitis*, *Staphylococcus lugdunensis*, *Staphylococcus warneri*, not differentiated), *Enterococcus faecalis*, *Enterococcus faecium*, *Streptococcus* spp. (*Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus gallolyticus*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, not differentiated), *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella* spp. (*Klebsiella pneumoniae*, *Klebsiella oxytoca*, not differentiated), *Escherichia coli*, *Enterobacter* spp. (*Enterobacter cloacae*, *Enterobacter* | Same |

| Similarities | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| | *(Klebsiella) aerogenes*, not differentiated), *Proteus* spp. (*Proteus mirabilis*, *Proteus vulgaris*, not differentiated), *Citrobacter* spp. (*Citrobacter freundii*, *Citrobacter koseri*, not differentiated), *Serratia marcescens*, *Candida albicans* and *Candida glabrata.* | |
| **Sample** | Positive Blood Culture as identified by a continuous monitoring blood culture system | Same |
| **Reagent Cartridge** | Accelerate PhenoTest™ BC kit | Same |
| **Instrument** | Accelerate Pheno™ system | Same |

Table 1: Predicate Device Comparison Differences

| Differences | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| **Antimicrobial Agents** | Double concentrations of aztreonam, cefepime, ceftazidime and piperacillin tazobactam for *Pseudomonas aeruginosa* testing | Single concentrations of aztreonam, cefepime, ceftazidime and piperacillin tazobactam |

| Differences | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| | Removal of MLSb and erythromycin | Included MLSb and erythromycin |
| **Test Kit** | Accelerate PhenoTest™ BC kit, enhanced wet reagent well (consolidated wells) | Accelerate PhenoTest™ BC kit, wet reagent well |
| **External Quality Control Assays** | Accelerate PhenoTest™ BC ID and AST QC test(s) | Manual QC assay |
| **ATCC QC Organisms Maintenance** | No QC organism maintenance required | Users required to maintain all 20 QC strains required for testing |
| **QC Sample Preparation** | Automated QC inoculum preparation and standardization performed by the Accelerate Pheno™ system | User prepares standardized inoculum of each QC strain and manually dispenses into designated wells in the Accelerate PhenoTest™ BC kit |
| **Accessories/Materials Required But Not Provided For External QC Testing** | Accelerate PhenoTest™ BC ID and AST QC test(s) | QC Assay Loading "Template Tool"<br>ATCC QC organism(s)<br>35°C (+/- 2) Incubator with $CO_2$<br>Trypticase soy agar (TSA) plates containing 5% sheep's blood (BAP) (for bacteria growth)<br>Sabouraud Dextrose plates (for yeast growth) |

| Differences | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| | | Commercially prepared Trypticase soy broth (TSB) with no additives<br>Commercially available, calibrated turbidity meter<br>0.5 and 2.0 McFarland Standards for use with commercially available turbidity meter<br>Falcon® 5mL Round Bottom Polystyrene Test Tubes with Snap Cap, Sterile (Corning Product # 352054) or equivalent |
| **Test Interpretation and Results Reporting** | Modified Expert rules | Original Expert rules from DEN160032 |
| | ID Interpretive Rules increase reporting of the monomicrobial call and decreases incidence of indeterminate calls and ambiguous results due to debris/noise | Original Monomicrobial Indeterminate and false positive in DEN160032 |
| | AO Bright Rule improves overall reportability by decreasing invalid results | Original invalid results in DEN160032 |

| Differences | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| | Noise Rejection analysis decreases by-run false positive rate of clinical stock isolates | By-run false positive rate for clinical stock isolates in DEN160032 |
| | Improved ID target detection thresholds | Original normal hit, bright rule and high sensitivity detection in DEN160032 |
| | MEM algorithm changes decrease MIN error rate for PAE | Original MIN error rate for PAE |
| **Time to Result** | ID Results ~2 hours<br>AST Results ~7 hours | ID Results ~1.5 hours<br>AST Results ~6.5 hours |
| **Instrument** | Optical set submitted in DEN160032 with additional far-red filter | Optical set submitted in DEN160032 |
| **Computing System** | Add Interface PC/Analysis module setup (supports up to 8 ID/AST modules) | Control PC/Analysis PC setup (supports up to 4 ID/AST modules) |
| **Software Algorithms** | Add ID interpretive rules, AO bright rule, and ID algorithm improvements. Updated algorithms for aztreonam, cefepime, ceftazidime, meropenem and piperacillin-tazobactam with *P. aeruginosa* | Original algorithms for aztreonam, cefepime, ceftazidime, meropenem and piperacillin-tazobactam with *P. aeruginosa* |
| **Software Algorithms** | Accelerate Pheno™ system software includes noise rejection analysis using far red filter to reject interfering debris | Noise rejection analysis using far red filter to reject interfering debris not performed |

| Differences | | |
|---|---|---|
| **Item** | **Device**<br>**Accelerate PhenoTest™ BC Kit** | **Predicate**<br>**Accelerate PhenoTest™ BC Kit (DEN160032)** |
| **Software QC Assays** | Accelerate Pheno™ system software automates QC testing for ID and AST using the Accelerate PhenoTest™ BC ID/AST QC tests | QC assays performed by Accelerate Pheno™ system requires manual dispensing of standardized inoculum into designated wells of Accelerate PhenoTest™ BC kit |

**Performance Data**

Performance data are provided within this premarket notification in support of the substantial equivalence determination.

**Electrical safety and electromagnetic compatibility (EMC)**

Electrical safety and EMC testing is identical to that conducted for the predicate device. The Accelerate Pheno™ system complies with IEC 61010-1:2010, Safety requirements for electrical equipment for measurement, control, and laboratory use- Part 1: General requirements, and also with IEC 60601-1-2:2014, medical electrical equipment: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances – Requirements and tests.

**Software Verification and Validation Testing**

Software verification and validation testing were conducted and documentation is provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered to have a "moderate" level of concern, since a failure or latent flaw could indirectly result in minor injury to the patient or operator through incorrect or delayed information or through the action of a care provider.

**Non-Clinical Test Summaries**

**Performance Evaluation**

Performance of the modified Accelerate PhenoTest™ BC kit aztreonam (ATM), ceftazidime (CAZ), cefepime (FEP), meropenem (MEM) and piperacillin-tazobactam (TZP) *Pseudomonas aeruginosa* assays was established during an internal performance evaluation study at Accelerate Diagnostics, Inc. A total of 131 characterized *Pseudomonas aeruginosa* isolates were tested at the internal site in two phases along with evaluation of the new algorithms on the original 13 clinical trial isolates for a total of 144 isolates included in the performance evaluation. Phase 1 included testing of 100 challenge and stock isolates (115 total runs), and Phase 2 evaluated an additional 31 on-scale isolates. *P. aeruginosa* isolates were seeded into BD BACTEC™ Plus Aerobic blood culture bottles containing healthy donor blood and incubated until positivity on the BD BACTEC™ system. Samples from positive blood culture bottles were Gram-stained, run on the Accelerate Pheno™ system, sub-cultured for purity on trypticase soy agar (TSA) plates, and images were taken with Sphere FLASH®. Antimicrobial susceptibility test (AST) results were compared to historical results from the broth

microdilution (BMD) reference method. Quality control testing for the Accelerate PhenoTest™ BC kit was performed daily using the Accelerate PhenoTest™ BC ID and AST QC tests.

During the Phase 1 performance evaluation study, a total of 113 out of the 115 tested samples produced a positive identification for *Pseudomonas aeruginosa*. Two of the *P. aeruginosa* samples produced negative or off-panel ID calls and were excluded from analysis per study exclusion criteria. Of the 113 positive *P. aeruginosa* samples, 13 did not proceed to AST testing due to invalid results (e.g., growth control channel failures) and were additionally excluded from data analysis. In Phase 2, aside from five isolates that were retested once each due to ID failures, all experiments resulted in valid data points for all five beta lactam antimicrobials.

The primary objective of the clinical evaluation study for the Accelerate PhenoTest™ BC kit aztreonam, cefepime, ceftazidime, meropenem and piperacillin-tazobactam *Pseudomonas aeruginosa* assays was to produce adequate essential and categorical agreement. At least two two-fold dilutions below the susceptible and one two-fold dilution above the resistant threshold as specified in the FDA Class II Special Controls Guidance document were tested over the Accelerate Pheno™ system reportable ranges of ≤2 µg/mL to ≥64 µg/mL (ATM, CAZ, FEP), ≤1 µg/mL to ≥16 µg/mL (MEM), ≤4 µg/mL to ≥256 µg/mL (TZP). Table 3 provides an overall summary of AST performance for the two testing phases plus analysis of the 13 original clinical isolates for the Accelerate PhenoTest™ BC kit aztreonam, cefepime, ceftazidime, meropenem and piperacillin-tazobactam *Pseudomonas aeruginosa* assays.

Table 2: Accelerate PhenoTest™ BC kit Assay Performance Summary

| Abx | Reporting Range | N | #EA | %EA | N (Eval) | #EA (Eval) | %EA (Eval) | #CA | %CA | #R | #S | #vmj | %vmj | #maj | %maj | #min | %min |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ATM[a] | 2-64 | 144 | 135 | 93.8 | 73 | 64 | 87.7 | 134 | 93.1 | 35 | 105 | 0 | 0 | 1 | 1.0 | 9 | 6.3 |
| FEP[a,b,d] | 2-64 | 143 | 136 | 95.1 | 40 | 33 | 82.5 | 132 | 92.3 | 36 | 107 | 1 | 2.8 | 10 | 9.3 | N/A | N/A |
| CAZ[a,c] | 2-64 | 141 | 136 | 96.5 | 30 | 25 | 83.3 | 136 | 96.5 | 38 | 103 | 3 | 7.9 | 2 | 1.9 | N/A | N/A |
| MEM[a,d,e] | 1-16 | 144 | 136 | 94.4 | 25 | 17 | 68.0 | 127 | 88.2 | 25 | 102 | 0 | 0 | 2 | 2.0 | 15 | 10.4 |
| TZP[a] | 4-256 | 138 | 133 | 96.4 | 27 | 22 | 81.5 | 130 | 94.2 | 30 | 101 | 0 | 0 | 0 | 0 | 8 | 5.8 |

[a]Using an expanded reference range, EA was reduced as follows due to lack of EA for very high or very low MICs: aztreonam 91.0%, ceftazidime 92.2%, cefepime 83.2%, piperacillin-tazobactam 93.5%, meropenem 93.1%.

[b]The observed major and very major error rates for cefepime when testing *P. aeruginosa* are 9.3% and 2.8% respectively. Based on the essential agreement and lack of an intermediate breakpoint for cefepime, the adjusted major error rate is 1.9% and the adjusted very major error rate is 0%.

[c]The observed very major error rate for ceftazidime when testing *P. aeruginosa* is 7.9%. Based on the essential agreement and lack of an intermediate breakpoint for ceftazidime, the adjusted very major error rate is 2.6%.

[d]When not in exact agreement, cefepime and meropenem MIC results for *P. aeruginosa* tended to be at least one doubling dilution higher than the reference method, which increases the potential for major errors.

[e]The observed low category agreement was due to the occurrence of a high number of minor errors.

AST performance met all acceptance criteria for aztreonam and piperacillin-tazobactam. For ceftazidime, all acceptance criteria were met except for the very major discrepancy rate, which was 3/38 (7.9%). However, based on the essential agreement and lack of an intermediate breakpoint for ceftazidime, the adjusted very major error rate is 2.6%. For cefepime, all acceptance criteria were met except for the very major and major discrepancy rates, which were 1/36 (2.8%) and 10/107 (9.3%), respectively. However, based on the essential agreement and lack of an intermediate breakpoint for cefepime, the adjusted major error rate is 1.9% and the adjusted very major error rate is 0%. Meropenem met all AST acceptance criteria except for categorical agreement at 127/144 (88.2%). Low categorical agreement for meropenem was attributed to the occurrence of a high number of minor errors. Daily quality control test results were all within the expected MIC range for each of the five antimicrobials.

**Reproducibility Testing**

An internal reproducibility study was conducted according to FDA's AST Class II Special Controls guidance. Isolates were selected such that the complete set contained at least ten isolates per antimicrobial (aztreonam, cefepime, ceftazidime, meropenem and piperacillin-tazobactam) whose modal MIC result could be expected to be on-scale. Isolates were cultured from frozen stock and used to spike blood culture bottles. Bottles were incubated until positive on a BD BACTEC® blood culture monitoring system. On each day of testing, three samples from the same positive blood culture bottle were run on three separate Accelerate Pheno™ systems. The same three systems were used for each isolate on all days of testing. Positive blood cultures were additionally sub-cultured for purity on trypticase soy agar plates, which were incubated at 35˚C for 18-24 hours. QC testing was conducted on each day of reproducibility testing using the Accelerate PhenoTest™ BC AST QC test. Best and worst-case EA rates were calculated for each antimicrobial-isolate combination as well as for each antimicrobial across all isolates whose modal MIC result for the same antimicrobial was on-scale. Best-case EA rate with the modal result was expected to be at least 95%.

As shown in Table 4 below, reproducibility was ≥95% for all antimicrobials with *P. aeruginosa*, with the exception of piperacillin-tazobactam. For this antimicrobial, two *P. aeruginosa* isolates were found to be highly variable in their response to piperacillin-tazobactam. Removal of these isolates provided 96.4% best case and 93.3% worst case results. All daily QC runs produced passing results.

Table 4: Reproducibility of AST assay for *P. aeruginosa* with beta lactams; Best and Worst Case Reproducibility

| Antibiotic | Best Case Totals | Best Case Percentage | Worst Case Totals | Worst Case Percentage |
|---|---|---|---|---|
| Aztreonam | 171/180 | 95.0% | 165/180 | 91.7% |
| Ceftazidime | 143/150 | 95.3% | 134/150 | 89.3% |
| Cefepime | 175/180 | 97.2% | 175/180 | 97.2% |
| Meropenem | 115/120 | 95.8% | 105/120 | 87.5% |
| Piperacillin-tazobactam[a] | 180/195 | 92.3% | 175/195 | 89.7% |

[a]Two *P. aeruginosa* isolates were found to be highly variable in their response to piperacillin-tazobactam; removal of these isolates provided the following reproducibility results: best case 96.4%, worst case 93.3%.

**Clinical Study Summary**

No clinical testing was performed to support a substantial equivalence determination for the aztreonam, cefepime, ceftazidime, meropenem and piperacillin-tazobactam assay modifications.